VOLUME LX JANUARY, 1950 NUMBER 1

THE LARYNGOSCOPE

FOUNDED IN 1896
BY
MAX A. GOLDSTEIN M. D.

PUBLISHED BY
THE LARYNGOSCOPE
640 SOUTH KINGSHIGHWAY ST. LOUIS (10), MO., U. S. A.

NOTICE TO CONTRIBUTORS

THE LARYNGOSCOPE reserves the right of exclusive publication of all articles submitted. This does not preclude their publication in Transactions of the various Societies.

Manuscripts should be typewritten, double spaced, on one side of paper only and with sufficient margins to allow for corrections.

References should be complete: author's surname, initials, title of article, journal, volume, page, month, year.

Six illustrations will be furnished for each article without cost to author. Authors will please limit illustrations to six or assume the expense of additional illustrations.

Proofs will be submitted to authors for corrections. If these are not returned, articles will be published as corrected in this office.

Reprints will be furnished at the following prices:

WITHOUT COVER

	250 Copies	500 Copies	1000 Copies	2000 Copies
Four Pages	$10.25	$12.00	$15.50	$24.00
Eight Pages	20.75	25.75	35.00	52.25
Twelve Pages	31.00	40.00	57.00	89.00
Sixteen Pages	40.50	49.00	65.50	98.00
Twenty Pages	48.00	58.75	79.50	121.00
Twenty-four Pages	58.00	70.50	95.00	143.50
Thirty-two Pages	76.75	91.25	121.25	179.00

WITH COVER

Four Pages	$19.00	$23.75	$33.25	$53.25
Eight Pages	29.50	37.50	52.75	81.50
Twelve Pages	39.75	51.75	74.75	118.25
Sixteen Pages	49.25	66.75	83.25	127.25
Twenty Pages	56.75	70.50	97.25	150.25
Twenty-four Pages	66.75	82.25	112.75	172.75
Thirty-two Pages	85.50	103.00	139.00	208.25

Express charges to be paid by consignee.

THE
LARYNGOSCOPE.

VOL. LX JANUARY, 1950. NO. 1

HISTIOCYTIC GRANULOMA OF SKULL.*

(A Triphasic Clinicopathologic Syndrome Previously Termed Letterer-Siwe's Disease, Hand-Schüller-Christian's Disease, and Eosinophilic Granuloma.)

Report of 18 Cases.

VICTOR GOODHILL, M.D.,
Los Angeles, Calif.

INTRODUCTION.

Histiocytic granuloma of the skull is a clinicopathologic entity which may appear in an acute, usually fatal form known as Letterer-Siwe's disease, a subacute serious stage known as Hand-Schüller-Christian's disease, and a chronic benign state known as eosinophilic granuloma.

Confusion reigned for several years as pathologists and clinicians diligently attempted to classify each one of the above phases into a separate distinct disease category.

Evidence will be presented to clarify the relationship between these three "diseases" and to demonstrate the fact that they are truly different phases of one single disease process, histiocytic granuloma.

*Submitted as Candidate's Thesis to the American Laryngological, Rhinological and Otological Society, Inc., 1948.

Editor's Note: This ms. received in Laryngoscope Office and accepted for publication, July 1, 1949.

Of great interest to the otolaryngologist is this disease with its frequent manifestations of otorrhea, temporal bone destruction, multiple skull erosions, proptosis, and diabetes insipidus.

The important contributions to the literature are summarized and 18 new cases are reported, illustrating the three phases of the disease.

HISTORICAL ASPECTS AND DEVELOPMENT OF PREVIOUS CONCEPTS.

I. Development of the Concept of Hand-Schüller-Christian's Disease.

In 1893, Alfred Hand published the report of a case showing a clinical triad of calvarial osseous defects, exophthalmos and polyuria in a three-year-old child. Because of the caseous-like appearance of the granulation process, Hand attributed the disease to tuberculosis and entitled his publication, "Polyuria and Tuberculosis." He felt that tuberculous deposits in the calvarium and skull base were associated with symptoms of polyuria.

In 1915, Arthur Schüller presented his concept of the disease. He described three cases, in each of which there were irregular defects in the membranous bones. His first case was that of a 16-year-old boy with infantilism, exophthalmos and the adiposogenital syndrome; the second case was that of a female, age four, with stunted growth, exophthalmos and diabetes insipidus; and the third case was an adult with skull lesions and an infiltration of the skin with yellow nodules. He did not make any suggestions regarding the etiology or pathology of the disease, but he simply pointed out the common radiological fact of irregular skull defects in all three cases; however, in 1926, Schüller felt that the disease was of pituitary origin and proposed the name "dysostosis hypophysaria."

In 1919, Henry Christian published an article entitled, "Defects in the Membranous Bones, Exophthalmos and Diabetes Insipidus." He reported the case of a five-year-old girl with

the triad mentioned and suggested that the diabetes insipidus was due to a disturbance of pituitary function. Then he pointed out that the polyuria was controlled by pituitrin intramuscularly.

In 1921, Hand reported another case in which he described a three-year-old child with exophthalmos, polyuria and an area of softening in the center of the right parietal bone. In this case again, as in 1893, Hand attributed the disease to tuberculosis, but he stated: "The primary process might be neoplastic, benign and myxomatous in character, affecting, for some unknown reason, the membranous bones and producing exophthalmos and polyuria secondarily by pressure." The pathological report mentioned the fact that there was a defect in the center of the right parietal bone occupied by a soft yellow material resembling the cavitation seen in tuberculosis.

In none of the publications by the above three authors, whose names have been linked to create a new disease entity (Hand-Schüller-Christian's disease), was there any distinct pathological description which would in any way fit the common present conception of the disease. None of the three men succeeded in actually presenting the features of a granulomatous lesion of lipoid character, perhaps of histiocytic origin.

In 1925, Thompson, Keegan and Dunn presented a case report of a nine-year-old boy with the classical triad: exophthalmos, calvarial defects and polyuria. In describing the autopsy findings, it is stated: "In the center of the largest membranous area, that is, the calvarial defect, there was yellowish fibrous tissue; and the inner surface of the dura mater was mottled by a yellowish tissue. Microscopic examination of the area showed a lining layer of large oval cells with sharp borders and clear, slightly granular cytoplasm and small, compact, centrally placed nuclei. The cytoplasm contained a variable amount of lipoid material in finely divided form." This was the first time in the history of the disease in which the existence of lipoid in the lesion was described.

Suffice it to say that the concept of the triad known today as Hand-Schüller-Christian's disease stems from the original reports of these three pioneer investigators, whose fine observations and keen clinical judgment justified the attachment of their names to this newly recognized entity, in spite of the fact that they did not describe the basic histopathologic features of the disease.

It remained for Dr. R. S. Rowland, in 1928, to correlate the various findings and to clarify the histopathology of the syndrome for the first time. He concluded that this syndrome of Hand, Schüller and Christian consisted of a form of xanthoma in which portions of the reticuloendothelial system became the site of excessive lipoid storage with resulting hyperplasia of lipoid-containing cells. He stated, "One is not dealing with true neoplasm but with hyperplastic new formation, *i.e.*, lipoid storage tumors. Formation of these nodules is a compensatory act on the part of the body in its attempt to rid the blood of an excess of lipoid which cannot be properly excreted." It was probably Rowland who, for the first time, applied the name xanthomatosis to the Hand-Schüller-Christian syndrome and who first attached the disease to the reticuloendothelial system insofar as histopathology was concerned.

When one considers the vast group of confusing diseases variously termed lipoidoses, one is confronted by a confusingly large number of diseases to which men's names have been attached. In discussing the lipoidoses, in some instances chemical methods have been used to outline distinctions. Thus, the clinical condition known as Niemann-Pick's disease is considered to be that entity in which a lipoid of the lecithin or phosphatide type is deposited in the lymphovascular and hematopoietic tissue of the liver, spleen and bone marrow. Another disease is Gaucher's, in which the lipoid material is a cerebroside. Xanthomatosis is a lipoidosis in which the lipoid material is cholesterol. Tay-Sach's disease is a condition in which the essential feature is a phosphatide lecithin

lipoid accumulation in the tissues of the central nervous system. A great deal of quarreling and argument ensued in the literature for years regarding the differential diagnosis of these various lipoid diseases; and even today there is no unanimity among pathologists or among biochemists regarding the fine differentiation that has been accorded these various diseases.

Certain pseudoscientific criteria for the differentiation of these diseases have been set up with a resultant increase in confusion among clinicians and pathologists. Ludwig Pick, who has written a great deal on these diseases, stated in 1933 in a discussion of Niemann-Pick's disease and other so-called xanthomatoses that Hand-Schüller-Christian's disease was an essential xanthomatosis. He stated, "It occurs predominantly in Jews and as far as we know in the male sex." He continues, "The lipoid deposition here consists chiefly of cholesterin fatty acid esters. The accumulation of large storage cells is secondary to a very characteristic granulation tissue which has an outspoken tendency to conversion into fibrous scars." In further discussing the disease, he goes on to give the clinical aspects of the triad as described above; and in addition he states that there are growth disturbances, dystrophia adiposogenitalis; yellow-brown skin discoloration; dyspnea; cyanosis; enlargement of the liver, spleen and lymph nodes. He stated that the foam cells eventually cicatrized, especially in the liver. He mentioned the observation that there is a complete replacement of bone marrow by masses of foam cells with subsequent formations for granulomatous tissue, which in turn produces the bony defect noted Roentgenologically.

It is of passing interest that Pick demonstrates his ignorance of modern anthropology by making the bald statement that Hand-Schüller-Christian's disease occurs predominantly in the Jewish "race." (Present-day scientific anthropology denies the authenticity of a so-called Jewish "race.") In the present report of 18 cases, there are none in Jewish patients.

He also stated that it occurred only in the male sex; and in this series of 18 cases to be presented, there were seven females and 11 males.

Dr. John Fraser published a masterful analysis of the Hand - Schuller - Christian entity entitled, "Skeletal Lipoid Granulomatosis." He described it as a disease of the so-called reticuloendothelial system in which there occurred the formation of a lipoid granuloma. He went into great detail to describe the reticuloendothelial system in an attempt to prove the histological rationale for the depostion of lipoids into these various cellular areas and also in an attempt to explain formation of some of the unusual histological structures such as the foam cells and giant cells seen in this disease. In describing the reticuloendothelial system, Fraser repeated the old concept that the system included the endothelium lining blood and lymph vessels. He then went on to mention the usual reticulum cells, the histiocytes and the monocytes in the blood stream. (He ignored the Maximow concept which is today more universally accepted; namely, that the reticuloendothelial system is a misnomer inasmuch as the reticulum cell, or histiocyte, is not related morphologically or developmentally with the endothelial cell lining of blood and lymph vessels. Maximow and Bloom stated that the most appropriate name for this type of cell form was the "histiocyte.")

Fraser, in pursuing his original thesis that Hand-Schüller-Christian's disease was a skeletal lipoid granulomatosis in which cholesterol was being absorbed and stored by the reticuloendothelium or histiocytic system, felt that hypercholesteremia was a very important factor in the production of this disease. He felt that an excess of lipoid in the circulating blood was due to a failure of the liver and lung tissue to maintain the body lipoid at a normal level.

Accordingly, it was his thesis that the reticuloendothelial tissue attempted to eliminate the excess by a process of absorption and deposit. This deposition of lipoid, according to Fraser, produces a considerable cell reaction in the reticu-

lar condition concerned; and it is this cellular reaction which produces the characteristic pathology of the lesion. In speculating upon the mechanism of the granulomatous formation, Fraser stated as follows: "The formation of the granulation elements is associated with certain untoward results. Its ability to infiltrate is insignificant, but it spreads with relative ease into parts occupied by areolar tissue and such fat-containing areas as the orbit and the perivascular spaces. What appears to be an infiltration of an organ is an extension along perivascular channels, and it is evident that fibrous tissue presents an impenetrable barrier to its invasion. Its progress in bone is marked by a progressive and extensive decalcification of trabecular and later compact bone with the result that large portions of the calvaria, clavicles or mandible—all more or less membrane bones—may disappear; and from what we find, it seems that the process of bone removal is one of osteolysis or phagocytosis initiated and accomplished by the larger type of multinuclear giant cell which is universally found at the periphery of the lesion. It is significant that, although large areas of bone may be involved and the skull wall reduced to a condition which has been described as gelatinous, the underlying dura and the overlying scalp often remain unaffected. The deposits in the basal subdural area are rare except for the space which lies around the hypophysis. This area is so frequently affected that it may be regarded as a site of election, and in some instances the sella turcica is filled with a putty-like mass with the result that there is displacement of the hypophysis and traction or pressure on its stalk. In a few instances, infiltration of the hypophysis and of the hypothalmic area has been described, but such is rare. It is a remarkable feature that, though there may be pronounced accumulation in the sella turcica, there is no invasion of the basisphenoid or of the clinoid processes.* From the hypophyseal fossa, the granulation tissue extends forward around the carotid vessels and then to the tissue around the optic nerve, until it finds itself in the orbit where factors of space and fat content permit such accumulation of

*This has not been true in my case reports.

the deposits and the eyeball is displaced. The effect of the disturbance in regions other than bone is a displacement process. Surrounding elements are pushed aside, depressed and atrophied. Tissue spaces are filled and distorted; and as far as can be observed, it is only in relation to bone that one witnesses the phagocytosis which so intimately affects the skeletal outline. The summary of the pathology is, briefly, that in certain tissue areas there is a formation of granulation tissue of distinctive cytology, the result of reactive changes in the reticuloendothelial tissue, the process being a reaction to a cholesterol excess in the blood and body fluids."

Fraser, in his clinical discussion, tended to oversimplify the disease; and in his anxiety to define clearly the limits of the disease as a lipoid granuloma, he perhaps was a little too enthusiastic in some of his conclusions. He states, "The blood readings show an excess of cholesterol, of total acids and of lecithin. The characteristic histological picture is a proliferation of the reticuloendothelial cell groups, illustrating the presence of large numbers of phagocytic cells, multinucleated giant cells and large lipoid-containing or foam cells."

John Fraser's contribution to our conception of this disease was monumental.

Following the clear-cut descriptions of the above-mentioned authors, numerous publications quickly began to appear in the literature, particularly in the pathologic, radiologic and otolaryngologic fields.

In 1938, Shea reported one case of xanthomatosis which responded to X-ray therapy.

In 1932, M. C. Sosman discussed the subject of xanthomatosis and added two new cases.

In 1935, Lederer, Poncher and Fabricant added one case report to the literature. It was an instance of temporal bone involvement without otorrhea where the only findings were those of a granuloma in the external auditory canal and calvarial involvement. The process was favorably reversed by X-ray therapy.

In 1936, J. G. Druss reported a case of temporal bone involvement by Hand-Schüller-Christian's disease in a 48-year-old man. The patient had no otorrhea but had diabetes insipidus. The temporal bone section showed involvement, but it was discovered accidentally on routine temporal bone studies. There were no clinical manifestations during life.

In 1937, V. V. Wood presented a case of bilateral mastoid involvement by xanthomatosis.

In 1940, D. S. Kellogg presented one case report of a parietal lesion that was palpable physically and seen on X-ray. There was no temporal bone involvement. There was no biopsy. A diagnosis of xanthomatosis was made purely on the response of the parietal lesion to X-ray therapy.

In 1946, M. A. Glatt presented a patient with otorrhea who had other evidence of Hand-Schüller-Christian's disease.

In 1940, Rosenwasser reported an interesting case of a patient who had been diagnosed as having a temporal bone neoplasm called carcinoma simplex. The tissue was re-examined four years later and rediagnosed as xanthoma. The patient responded well to X-ray therapy.

In December, 1938, R. L. J. Kennedy reported eight cases of Hand-Schüller-Christian's disease from the Mayo Clinic. All of these patients had demonstrable skull defects; none of them had changes chemically in the blood lipoids. All of the patients were either improved or entirely well when last heard from. The treatment of choice in all these cases was the local application of X-ray or radium in small suberythema doses. Gradually, the author reports, the defects in bone were replaced by normal bone which obliterated in most instances all evidence of the original lesion.

In 1939, Cooper reported the case of a 13-year-old child with diabetes insipidus and a postauricular abscess which responded to surgical drainage and postoperative X-ray therapy.

In 1940, Hamblen, Arena and Cuyler reported one case of Hand-Schüller-Christian's disease in which urinary androgens were studied. These androgen excretions amounted to 10 times the normal value. It was felt that this was due to the general disturbance of lipid metabolism and not due to any hypercortical or hypergonadal activity.

Many of the specific manifestations of Hand-Schüller-Christian's disease have been subjected to careful clinicopathological study. For example, ocular symptoms were very thoroughly analyzed in 1933 by Sanguinetti, who stated that the pathogenesis of the exophthalmos is based upon deformation of the orbit due to softening and rarefaction of the bony walls. The bony floor of the cranium may be converted into a membrane which is depressed by the weight of the overlying cerebral mass and results in flattening of the orbital cavity, compression of the optic nerve and partial atrophy. Pressure also displaces the eyeball and results in exophthalmos.

Carl Behr, in 1936, in another study of the ophthalmologic changes in Hand-Schüller-Christian's disease, tried to subdivide the various lipoidoses insofar as their ocular manifestations are concerned. He reported a monosymptomatic circumscribed instance in which an orbital involvement followed trauma and in which the patient recovered completely following surgical extirpation of the mass. He was able to demonstrate a hypercholesteremia in this patient and noted the interesting observation that here was a man of 69 years who, in spite of hypercholesteremia and Hand-Schüller-Christian's disease, did not have any evidence of generalized arteriosclerosis.

Lane and Smith, in the discussion of the cutaneous manifestations of chronic idiopathic lipoidosis, or Hand-Schüller-Christian's disease, report four cases. According to their studies, cutaneous manifestation are present in only one-third of the cases of Hand-Schüller-Christian's disease. According to these authors, there are two common types of eruption in this disease: the petechial and the diffuse papular. It seems that the diffuse petechial hemorrhagic eruption occurs in

severe and acute cases; whereas with protracted disease, papular or nodular lesions may appear. The papules are at first bright red but later assume a yellow or brown color from the xanthomatous deposits in the skin. The petechial exanthem would indicate that in the more fulminating types there is damage to the capillaries with hemorrhages into the skin. These authors feel that the skin manifestations should be studied more closely inasmuch as they may very well be diagnostic in the absence of the complete triad of exophthalmos, polyuria and calvarial lesions.

Slesinger, in 1936, reported a fatal case in a three-year-old child whose chief complaint on admission was a swelling in the postauricular region. There was no otorrhea. There were no other significant findings. A section was reported from the biopsy of the postauricular mass as showing a peculiar form of granulation tissue with many polyhedral cells that had the appearance of being histiocytes. Further biopsy was reported as showing essentially the findings of lipoid histiocytosis. The child was given deep Roentgen ray therapy, but there did not seem to be any response to treatment; however, a direct implantation of radium into the postauricular lesion produced complete healing within three weeks. Within several months, new lesions appeared in lymph nodes, in the left parietal region and in the right knee; finally, polyuria and polydipsia appeared. At no time was there any exophthalmos.

Wynkoop and Hadley, in 1938, reported a case of a child with numerous skeletal lesions but no exophthalmos or diabetes insipidus. He apparently made a complete recovery following diffuse X-ray therapy.

Rudolph Klotz, in 1940, describes one case, termed by him as Christian's syndrome rather than Hand-Schüller-Christian's disease because of the fact that only a geographic skull was found. This patient, in addition to a parietal lesion, also had a splenic tumor and a disturbance of liver function. The author considered that this was a case of monosymptomatic "Christian's" disease.

Robert Strong, in 1936, reviewed the literature and stated, "Xanthomatosis may be regarded as being a clinical disease due to a disturbed lipoid metabolism which is not necessarily related to the general metabolism of fats, but is, in a large measure, influenced by the part played by the reticuloendothelial system.

In 1936, Dauksys reviewed the literature to date and reported one case.

In 1935, Teperson reported the case of a 16-month-old child with proptosis, later followed by other cranial defects; no diabetes insipidus appeared in this child. X-ray therapy was apparently successfully used.

II. Development of the Concept of Letterer-Siwe's Disease.

In 1936, Abt and Denenholz published a paper in which they proposed the name "Letterer-Siwe's disease" for a clinical entity of "splenohepatomegaly associated with widespread hyperplasia of the nonlipoid storing macrophages." They gave credit to E. Letterer and S. A. Siwe for earlier descriptions of clinical characteristics and pathological definitions.

In a lucid description of this entity, Tracy B. Mallory states, "Typical Letterer-Siwe's disease rarely occurs beyond two years of age and runs a rapidly and, it is at present believed, inevitably fatal course. It is characterized clinically by fever, skin rash, rapidly progressive anemia and purpura, and histologically by marked proliferation of the so-called 'reticuloendothelial' (monocytic and clasmatocytic) cells in many parts of the body, particularly the skin, lymph nodes and the spleen."

Letterer termed this "disease" aleukemic reticulosis. Siwe called it diffuse reticuloendotheliosis. Foot and Olcott suggested the term nonlipoid histiocytosis.

III. Development of the Concept of Eosinophilic Granuloma.

In 1940, Lichtenstein and Jaffe reported a case in which they stated as follows: "We propose that this lesion be desig-

nated eosinophilic granuloma of bone. It presents itself as a rather well localized single lesion starting in the medullary cavity and tending to erode, expand and perforate the cortex in the bone site affected. In microscopic appearance there are aggregates of large phagocytic cells with conspicuous collections of eosinophilic leucocytes interspersed." They suggested that this lesion may be a virus granuloma.

In the same year, Otani and Ehrlich described four cases of solitary bone lesions which seemed to be benign. They did not find any lipophages; therefore, they felt that they were not dealing with a "lipogranuloma of Hand-Schüller-Christian's. Because of the absence of doubly refractile fat, they ruled out the latter disease. Their histological studies showed a predominance of histiocytes and eosinophiles. They suggested that these granulomata are of traumatic origin.

In 1944, Jaffe and Lichtenstein made another contribution to the literature in which they reported several new cases and advanced the concept of nosologic independence of eosinophilic granuloma as a pathological and clinical entity. They made a very strong plea for the dissociation of this disease from the Hand-Schüller-Christian group. In discussing the histopathological picture, they stated as follows: "When an affected region of bone, not fractured, in which the lesion is in an early phase is entered, it is likely to be found more or less hemorrhagic and cystic and to show a relatively small amount of soft, brownish granulation tissue which may be streaked with yellow. Indeed, much of this granulation tissue may be found necrotic. Characteristically, the non-necrotic tissue represents, on microscopic examination, conspicuous sheet-like collections of large phagocytic cells of the nature of histiocytes, interspersed among which are more or less conspicuous numbers of eosinophilic cells and especially of eosinophilic leucocytes; furthermore, one finds actively phagocytic, multinuclear, giant cells especially in the vicinity of fields of hemorrhage and necrosis. *It is the histiocytes that constitute the basic component of the lesion.** Most of them contain a

*Italics are the present writer's.

single nucleus; a small number have two nuclei or even more. Nuclei are large and usually roundish; although some are oval, kidney-shaped, creased or otherwise modified in contour. In the cytoplasm of the uninuclear or multinuclear histiocytes, and also in the giant multinuclear cells, one often observes phagocytosed erythrocytes and granulocytes, usually eosinophiles, in various stages of disintegration as well as brownish hemosiderin granules."

They go on to state: "Particularly in the vicinity of the fields of necrosis, some of the unicellular and many of the multicellular or giant histiocytes may be found to contain sudanophilic droplets. These are not doubly refractile as a rule and apparently represent phagocytosed particles of the neutral fat naturally present in the invaded interior of the affected bone. The histiocytes are apparently derived from the multipotent reticulum cells in the adventitia of the blood vessels in the marrow. Indeed, in many of the lesions one finds evidence of clumping and multiplication of the adventitial cells of these vessels. In addition, one can note their apparent transformation into more roundish cells of the general size, shape and character of histiocytes and their close resemblance subsequently to the neighboring cells of the lesion, which are indubitably histiocytes exhibiting phagocytosis.

"The eosinophiles, though not a basic constituent of the lesion, yet give it a striking imprint especially when present in large numbers. For the most part these cells present irregular or bilobular nuclei; although in some lesions or in some places in a given lesion the nuclei of the eosinophilic cells were roundish and not indented."

In spite of their previous assertion as to the independence of eosinophilic granuloma as an entity, they wisely conclude: "Nevertheless, it is logically probable that the lesions of bones in Schüller-Christian's disease may originally resemble those of eosinophilic granuloma of bone. This assumption is based on the fact that, on the one hand, in the early stages of evolution of Letterer-Siwe's disease one may find destructive skele-

tal lesions resembling cytologically those of eosinophilic granuloma of bone, and, on the other hand, in its chronic stages Letterer-Siwe's disease takes on the aspect of Schüller-Christian's disease, the skeletal and even certain visceral lesions undergoing lipogranulomatous transformation."

Michael and Norcross, in 1945, reviewed the concept of eosinophilic granuloma. They also quote two previous cases which probably could have been classified as eosinophilic granuloma but which were not classified as such. One is the case of Finzi, in which there was a lesion in the frontal bone of a 15-year-old boy; and the other was described in a paper by Schairer, who reported two cases of frontal "osteomyelitis" with eosinophilic response.

They proceeded to set up the following 10 criteria for the diagnosis of eosinophilic granuloma. (It is obvious from their own criteria that eosinophilic granuloma is a phase in the disease including Letterer-Siwe's and Hand-Schüller-Christian's.)

1. It is a benign destructive lesion affecting principally the skeletal system, with a predilection for the ribs and skull.

2. It is no longer considered a solitary lesion, but rather frequently affects multiple osseous areas.

3. It has a unique histologic picture, consisting of large accumulations of histiocytes, eosinophilic cells, principally leucocytes, and giant cells. The giant cells are large, acidophilic and multinucleated, frequently containing phagocytosed eosinophilic granules, neutral fat droplets and debris. In addition, there are large cells of apparent osseous origin, probably osteoclasts, which are relatively few in number.

4. It has in Roentgenograms a suggestive, but not entirely diagnostic appearance. It involves primarily the interior of the bone, expanding and frequently eroding the cortex, and sometimes invading the adjacent soft tissues. This erosion also occasionally results in pathologic fractures.

5. The condition is practically limited to children and young adults, especially males.

6. Surgical treatment is the most desirable procedure, although the disease is amenable to X-ray therapy. Spontaneous healing, however, is known to occur, unassisted by any other therapy.

7. Although not proved, it is thought to be associated in some manner as a stage of Schüller-Christian's disease and Letterer-Siwe's disease, representing a different expression of the same basic lipoid disorder.

8. The cause is obscure, but is most probably the result of some infectious agent. The part played by trauma, as stressed by several authors, does not seem to be substantiated. Some obscure virus infection has also been postulated. As yet, the pathogenesis has not been established.

9. Recognition of the benignity of the lesion will result in a more conservative therapy in certain obscure bone lesions.

10. There may be a relatively long interval between the recognition of the initial lesion and appearance of subsequent lesions.

Weinstein, Francis and Sprofkin report a case with lesions in the skull, pelvis and lungs; and yet they termed it eosinophilic granuloma, in contradiction to the terms laid down by the proponents of the disease, Lichtenstein and Jaffe.

John Raaf, in 1945, reported the case of a six-month-old child with lesions in the skull and fibula which responded to surgical extirpation.

Bailey and Freis report one case of so-called eosinophilic granuloma with lesions in the mandible, parietal bone and rib. Again, it is difficult to see how such multiple lesions can be classified "eosinophilic granuloma."

Salomon and Engelsher reported one case of a solitary supraorbital lesion which they called destructive granuloma.

In 1944, Osborne, Freis and Levin reported one case of so-called eosinophilic granuloma of bone in the temporal bone and mandible, in which the lesion of the temporal bone was severe enough to produce facial paralysis, deafness and labyrinthine symptoms. This case responded to X-ray therapy. It is difficult to see how this case differs substantially from the case reported by Rosenwasser as Hand-Schüller-Christian's involving the temporal bone.

Bakody, in 1946, reported a massive lesion in the skull diagnosed as eosinophilic granuloma, which was treated surgically and by postsurgical radiation and in which a tantalum prosthesis was inserted to take care of the skull defect.

M. H. Bass, in 1941, reported two children, one with a skull and one with a rib lesion; both cases responded to X-ray therapy. He reported the difficulty of pathologists in reaching unanimity of diagnosis, one calling the section eosinophilic granuloma and another Hand-Schüller-Christian's disease.

Dundon, Williams and Laipply, in 1946, reported five new cases of "eosinophilic granuloma," all in extremities.

Hamilton *et al.*, in 1946, reported nine cases of eosinophilic granuloma in various parts of the body.

Riley, in 1946, reported one case with rib involvement.

Solomon and Schwartz, in 1945, reported one case with a femur lesion.

Horwitz, in 1943, reported a case with a solitary tibia lesion.

Kernwein and Queen, in 1943, reported one case with a femur lesion in which they state that "eosinophilic granuloma is a condition incompatible with Schüller-Christian's disease clinically because of the single lesion and the universally favorable course."

Weidman, in 1947, reported a number of cases of "eosinophilic granuloma of the skin" and stressed that they are probably unrelated pathologically to eosinophilic granuloma of bone.

DEVELOPMENT OF THE CONCEPT OF ONE DISEASE.

Wallgren, in 1940, reported two cases in infants in which he showed quite conclusively that nonlipoid reticuloendotheliosis and Schüller-Christian's disease were identical and, further, that infectious reticuloendotheliosis, Letterer's-Siwe's disease and Hand-Schüller-Christian's disease are all different types of the same malady.

In 1941, Dr. Sidney Farber, of Boston, in a discussion on "Solitary, or Eosinophilic Granuloma," considered the entire subject as advanced by Lichtenstein and Jaffe and stated that in his study of 10 children he could find no difference between the pathological picture in eosinophilic granuloma and that of Schüller-Christian's disease or Letterer-Siwe's disease. Farber felt that none of these three conditions could really be considered an xanthomatous process or a manifestation of a primary alteration in lipid metabolism. He concluded that his studies do not lend support to the conclusion that eosinophilic, or solitary granuloma of bone is either a new or a separate disease entity. If this suggestion concerning the nature of these benign bone lesions is correct, caution must be exercised in the prognosis because of the possibility of later visceral involvement.

In 1942, Green and Farber reported 10 cases of benign bone destruction in which they were Roentgenologically and histologically indistinguishable from Hand - Schüller - Christian's disease. They, therefore, reaffirmed their previous statement that eosinophilic, or solitary, granuloma of bone was a variant of Hand-Schüller-Christian's disease and not a new entity.

In 1942, Gross and Jacox reported three cases and came to the conclusion that eosinophilic granuloma "is a reticuloendotheliosis and probably identical with those cases of Hand-Christian's disease which have been reported to have solitary lesions. It is also closely related to certain other reticuloendothelial hyperplasias."

In 1944, Versiani, Figueiro and Junqueira reported the case of a 50-year-old female with diabetes insipidus and a lesion in the femur. The histologic lesion in the femur showed a granuloma with two zones: *1.* an accumulation of eosinophiles giving the typical pictures of eosinophilic granuloma, and, *2.* lipophages, foam cells, arranged like a typical lipogranuloma as seen in Hand-Schüller-Christian's disease. They were, therefore, able to demonstrate in the same femur lesion the characteristic histologic findings of both eosinophilic granuloma and the Hand-Schüller-Christian type of xanthomatosis. They, accordingly, feel strongly that both are variants of the same disease.

In 1944, Engelbreth-Holm, Teilum and Christensen reported the detailed study of five children, aged two to nine years. All of these five children had been diagnosed at one time or another to have so-called eosinophilic granulomata of bone. The authors presented the following evidence to show that there was a gradual transition in the study of these cases from eosinophilic granuloma to Schüller-Christian's syndrome. In summarizing their work, they state:

"Clinically, transitions were formed from the solitary eosinophile granuloma through cases with several osseous foci to a generalized case with innumerable foci in the bone system together with diabetes insipidus, disturbance of growth and Roentgenographic changes in the lungs. In several cases where the disease commenced as a solitary granuloma, continued observation has revealed additional foci, so that in our material the number of foci increases with the length of the observation period.

"Morphologically, transitions were demonstrated from the lipoid-free eosinophile granuloma through granuloma with beginning lipoid phagocytosis with Touton cells to entirely xanthomatous tissue.

"After this, the concept eosinophile granulomas can no longer be maintained as a nosologic entity but must be con-

sidered a not altogether infrequent clinical monosymptomatic form of Schüller-Christian's disease that often heals without becoming generalized.

"Complete agreement is demonstrated between the various histological pictures in the cases of eosinophile granulomas here described and the various histogenic phases of Schüller-Christian's disease that may be characterized as follows:

"*1.* The hyperplastic-proliferative phase.

"*2.* The granuloma phase.

"*3.* The xanthoma phase.

"*4.* The fibrous (or healing) phase."

In 1946, Imler reported two cases from the therapeutic radiologic standpoint. He designated the disease itself "reticuloendotheliosis" and felt that the separation of Hand-Schüller-Christian's disease, eosinophilic granuloma and Letterer-Siwe's disease into specific disease entities was not valid on the basis of the evidence at hand. He felt that there were insufficient data to support the claim of a lipoid-metabolic disorder as the primary causative factor. He considered that these diseases were all variants of a hyperplastic reaction of the reticuloendothelial system; for that reason, he gave it the name of reticuloendotheliosis. In discussing diabetes insipidus, he felt that the stage of the disease process in the hypophysis and tuber cinereum would determine the response of the diabetes insipidus to deep X-ray therapy. If the infiltration is in the stage of fibrosis, no, or little, improvement could be expected.

In 1947, S. J. Thannhauser attacked the concept of eosinophilic granuloma of bone as advanced by Lichtenstein and Jaffe on the following grounds:

He showed first that eosinophilic aggregations had been described in this syndrome on many previous occasions. He called attention to the work previously quoted here by John Fraser, in which the earlier stage, so-called lipogranuloma,

was manifested by endothelial proliferation and the accumulation of eosinophilic cells as well as giant cells. Thannhauser felt that the designation of the disease under discussion as eosinophilic granuloma was incomplete and therefore misleading, since "eosinophilic granuloma is not a disease entity but only a phase in the histologic aspect of a distinct clinical syndrome. The xanthoma cell formation in the later phases of the lesions is as characteristic of the disease as the reticulohistiocytic proliferation and the accumulation of eosinophiles in the earlier phases. If one does not prefer to use the older names, Schüller-Christian's syndrome or lipoid granulomatosis or normocholesteremic xanthomatosis, one should think of a classification which would at least refer to the principal two histologic phases of the granuloma; namely, a proliferative and eosinophilic phase and an xanthomatous phase. The designation of the localized and systemic disorder as eosinophilic xanthomatous granuloma seems to be more appropriate even if it does not embrace the reticulohistiocytic proliferation of the early lesion. Such a name would also prevent further misunderstanding in the conception and classification of this disorder.

"So-called eosinophilic granuloma of bone is certainly not a newly disovered disease entity but is the monosymptomatic form of the well known systemic granulomatous disorder in which histiocytes, eosinophiles and xanthoma cells are observed in the lesion at different phases."

Several months later, in December, 1947, Jaffe and Lichtenstein answered Thannhauser's criticism and defended the rationale employed by them in the setting up of the entity of eosinophilic granuloma. They pointed out the fact that "eosinophilic xanthomatous granuloma," which Thannhauser proposed as a comprehensive name for all cases, has the disadvantage that lesions of eosinophilic granuloma and of Letterer-Siwe's disease may be practically devoid of lipid; while, on the other hand, lesions of clinical Schüller-Christian's disease usually fail to show conspicuous eosinophilic reaction. "Whatever the anatomic interrelations may be, a case present-

ing an eosinophilic granulomatous lesion in one bone only (not a calvarial bone) without manifestations of general disease and in which simple curettage leads to complete healing of the condition has no clinical affiliation with cases of Schüller-Christian's disease. A simple analogy is in order. Miliary tuberculosis and active tuberculosis limited to a knee joint have the same bacterial cause, but they are decidedly different conditions from the clinical point of view. In the same way, though eosinophilic granuloma of bone and Letterer-Siwe's and Schüller-Christian's disease apparently represent different phases of the same basic disorder, there is a need for retaining at least clinical distinction between them."

They state further: "Even if it were to be demonstrated that some lesions of eosinophilic granuloma subsequently undergo transformation to lipoid granuloma, it still would make good sense on clinical grounds to segregate cases of eosinophilic granuloma, which is usually limited to one or a few bones and always runs a benign course, from cases of Schüller-Christian's disease, which often proves fatal and in which there are often pulmonary, cerebral or other visceral lesions in addition to skeletal involvement."

It is obvious, therefore, that, in 1947, Lichtenstein and Jaffe feel that the primary excuse for retention of the term "eosinophilic granuloma" is for a clinical distinction; and they, in fact, imply their agreement with the concept of a single disease which may have different clinical expressions during certain phases of the process.

Curtis and Cawley, in 1947, felt that the term "Hand-Schüller-Christian's disease" should be withdrawn from the diseases of lipid metabolism, the remaining members of which are Gaucher's and Niemann-Pick's. They feel that there are three related diseases; namely, Letterer-Siwe's, Hand-Schüller - Christian's and eosinophilic granuloma. They consider them all various forms of the same disease. They again mention the fact that Letterer-Siwe's disease is more common in infants; is severe; and is characterized by large skull

defects, fever, hepatomegaly, splenomegaly, severe skin manifestations and high mortality. They go on to describe Hand-Schüller-Christian's disease as being characterized by skull lesions, diabetes insipidus, exophthalmos and skin manifestations in one-third of the patients. They conclude that eosinophilic granuloma is a disease of solitary bone lesions.

Strauss, in a recent article in 1948, gives three case reports and concludes: "It appears clear that eosinophilic granuloma of bone and its congeners, Hand-Schüller-Christian's disease and Letterer-Siwe's disease, represent merging clinical variations of an essentially similar pathologic process best described collectively by the term 'inflammatory histiocytosis'."

PATHOLOGY.

Hand-Schüller-Christian's disease was not clearly delineated from a pathological standpoint by either Hand, Schüller or Christian. It remained for Rowland, in 1928, to put the pathological understanding of this syndrome on a relatively definite basis. It was he who pointed out the similarity between the three observers; it was his original observation that this syndrome was an abnormality of the reticuloendothelial system in which the characteristic pathological finding was an abundance of so-called foam or xanthoma cells containing the specific lipid, cholesterol. It was upon this basis that he felt justified in distinguishing the disease from other lipoidoses such as Niemann-Pick's and Gaucher's. The triad of proptosis, diabetes insipidus and skull bony lesions was of interest and of some value from the clinical standpoint only; however, many pathologists insisted upon using the triad as a basis for a pathological diagnosis. Pathologically, this triad is not a necessary requirement for that stage of histiocytic granulomatosis in which xanthomatosis of the cholesterol type is the outstanding microscopic finding; nevertheless, on the basis of Rowland's work, which was a brilliant piece of investigation, xanthomatosis became a synonym for Hand-Schüller-Christian's disease; and the pathological picture, of necessity,

included the triad, if possible, and the demonstration, microscopically of foam cells of the xanthoma type containing cholesterin.

The pathological picture of Letterer-Siwe's disease was never clearly defined; however, Abt and Denenholz described a *clinical syndrome* in which the outstanding features were high mortality, occurrence in early infancy, widespread reticuloendothelial proliferation throughout the body, fever, acuteness of the process, marked cutaneous manifestations, as well as visceral involvement by the reticuloendothelial dysplasia. Here the microscopic picture was described as being one where the outstanding feature was a so-called reticuloendothelial cell proliferation, the major finding being large clusters of reticulum cells with some giant cells and a very occasional foam cell plus scattered evidences of other cells, such as plasma cells, eosinophiles and polymorphonuclears. Here, again, we were given a picture which was primarily clinical and in which the pathological picture was not too clear-cut, as can be evidenced by the confusion existing in the minds of most capable pathologists, who, upon seeing a section of a lymph node or a bony lesion, will hedge for weeks and months before making a definite diagnosis. They will frequently state, "this appears to be a reticuloendothelial dyscrasia either of the Hand-Schüller-Christian or of the Letterer-Siwe type."

Finally, the proponents of the concept of eosinophilic granuloma state, as mentioned above, that they were describing a reticuloendothelial granuloma in which the predominant picture was histiocytic proliferation, but in which the characteristic accumulations of eosinophiles gave it a more or less individualistic status among these diseases, and on the basis of that finding, as well as the clinical impression that they were dealing with a monolocular disease primarily confined to the long bones, they advocated that the term eosinophilic granuloma be accorded true identification from the pathological standpoint.

In summary, therefore, we were told that Hand-Schüller-Christian's disease was a disease characterized primarily by xanthoma, or foam cells, containing cholesterin crystals; that Letterer-Siwe's disease was a disease characterized primarily by reticulum cell proliferation with occasional foam cells and occasional eosinophiles; and finally, the eosinophilic granuloma proponents, Lichtenstein and Jaffe, felt that they were dealing with a separate disease because, in addition to the histiocytic manifestation which was predominant, they also noted clusters of eosinophiles in their cases.

It is a widespread belief among pathologists today that one of the most difficult diseases to pigeonhole is the disease in which there is a question of xanthomatous or eosinophilic involvement of the reticuloendothelial system. It is probably due to no fault of the pathologists that this difficulty and confusion exists. It is quite obvious that the difficulty existed with the original descriptions of these three so-called clinico-pathological entities; and the problem confronting the pathologist is how to make a diagnosis which has in itself never been firmly established in the original description of the disease.

THE UNIFYING CONCEPT OF HISTIOCYTIC GRANULOMATOSIS.

Numerous references to "reticuloendotheliosis" as a suggested term for the inclusion of all three of the above entities have appeared. They have been cited above. It is quite obvious, not only from the clinical but also from the pathological standpoint, that all three diseases are diseases of the so-called reticuloendothelial system. In the first disease classified according to acuteness, Letterer-Siwe's disease, the primary manifestation is reticulum cell proliferation. In the subacute form of the disease, Hand-Schüller-Christian's variety, the outstanding pathological finding is that of foam or xanthoma cells. And in the third or most benign and most chronic state of the disease, the eosinophilic granuloma, the outstanding pathological finding is eosinophilic aggregation around a predominantly histiocytic or reticuloendothelial response.

The essential pathological description in all three cases is that of granuloma formation. The granuloma in each case is of a nonspecific variety. Neither tuberculosis nor syphilis has ever been demonstrated as an etiologic agent in any of these cases. Virus infection has been suspected but never proved as an etiologic factor. The giant cells that appear in these cases are ordinary foreign-body giant cells and are not in themselves at all diagnostic of the type of granuloma. It seems logical to choose a term which will embody the basic pathologic alterations and to begin to eliminate the unnecessary confusion of three "diseases," the first two being named after their original authors, which, while indeed laudable and justifiable, is certainly not a boon to scientific terminology; furthermore, to the pathologist who is anxious to find a cytological and tissue method of description, a term embodying the basic cell form, namely, reticuloendotheliosis, is certainly to be desired.

The term reticuloendotheliosis has been advocated by Imler, Mallory and many others; however, a number of years ago it was pointed out quite logically and conclusively that the so-called reticuloendothelial system was a misnomer. The cell type involved was the histiocyte first described by Aschoff. The histiocyte by description was the cell participating in the various functions of the so-called reticuloendothelial system.

According to Maximow and Bloom, the term reticuloendothelium is not suitable, first, because it refers to only one of the representatives of the system, namely, the reticulum cell; second, because it creates the incorrect impression that the endothelium of the common blood vessels also belongs to this system. In speaking of the histiocytic system, Maximow speaks of a group of cells found in connective tissue and elsewhere, cells which are nonmotile but which are able to phagocytose particulate matter and to store foreign substances brought to them in colloidal solution. At first, phagocytosing and storing elements were found in different organs and tissues and were described under different names in the various places of the body. Maximow states, "In the loose, irregularly

arranged connective tissue, they were called the resting wandering cells or clasmatocytes. In the lymphoid and myeloid tissues and in the red pulp of the spleen, the reticular cells were known to possess the same fundamental functional properties as the resting wandering cells; moreover, the flat cells which line the lymphatic sinuses of the lymph nodes and the venous sinuses of the bone marrow and the spleen were also found to act similarly. In the liver, the peculiar stellate or Kupffer's cells in the wall of the intralobular sinusoids and some of the cells lining the sinusoids of the suprarenal and the hypophysis were known to be endowed with a very marked power of phagocytosis and storage. The 'dust cells' of the lungs were called by this term because they showed the ability to take up particles of dust brought in with the inspired air. All these elements, although sometimes very dissimilar under physiologic conditions, react in a very similar if not identical way in response to certain stimuli. This led to the conclusion that they belong to one common large cell group which plays an important functional role in the body. The most appropriate name for these cells is histiocytes."

Accordingly, from the standpoint of correctness of terminology, it is proposed by the author that the term "histiocytic granuloma" be applied to the entire group of diseases variously characterized as Hand-Schüller-Christian's, Letterer-Siwe's and eosinophilic granuloma. The advantage of such a unifying concept is that it will clarify the apparently confusing picture illustrated not only in many of the bibliographic references but also in the cases cited above, where in a given patient it was possible to demonstrate clinical and histological features that would place the patient in either one, two or all three categories. The lack of true unity in each one of the three diseases and the lack of real differences between the three make it imperative that a more basic concept be employed, and that these three clinicopathologic divisions be maintained only as clinical names, if at all. Perhaps it would be wise to term the Letterer-Siwe's category the reticulum cell stage, or *acute histiocytic granuloma*. Hand-

Schüller-Christian's disease could then be termed the xanthomatous lipid-storing phase or *subacute histiocytic granuloma.* The solitary, chronic lesion of eosinophilic granuloma would then be termed *chronic histiocytic granuloma.* It would thus be possible to correctly classify many of these patients. Some of these children had not only diabetes insipidus, skull lesions and proptosis, to put them in the Hand-Schüller-Christian variety, but also had marked skin rashes and marked skeletal lesions to place them in the Letterer-Siwe's and eosinophilic granuloma classification. In almost every fatal instance it was possible to trace the pathological sequence of events relating to various stages in the histiocytic granulomatous response.

Pathologically, therefore, there should be only one disease, to the best of our present knowledge. Thus *histiocytic granuloma* could be termed acute, in the reticulum cell predominating phase, subacute, in the xanthomatous predominating phase, and chronic in the eosinophilic predominating phase. Clinical distinctions are of only little value. The disease has a markedly *random* and "helter-skelter" quality as evidenced by the geographic variety of the skull and extremity lesions. There are no two cases in which any true sequential or chronological order could be compared. The response of the histiocytic system is bizarre and unpredictable. Thus we see acute cases with and without bony or lymph node lesions. We see chronic cases with and without skeletal or sellar involvement. We see subacute cases with and without proptosis or skin lesions. Visceral lesions have been seen in every stage of the disease and have been absent in every stage of the disease, in varying patients.

The pathological findings in the various lesions are primarily due to pressure phenomena produced by the granulomatous process. It is interesting to note in the one available temporal bone section the resistance of the capsule of the bony labyrinth to invasion by the granuloma. All other bones in the body, including the tympanic ossicles, the annulus tym-

panicus and the entire mastoid and petron can be destroyed by this disease, but the bony capsule of the internal ear appears to be resistant.

DIAGNOSIS.

In making the diagnosis of histiocytic granulomatosis, for the sake of statistical value and in the interest of further research in the phases of this syndrome, it would be wise to attempt in each case, wherever possible, to allocate it to one of the three stages of the disease or to two of these, whenever that becomes necessary. The diagnosis of the classical reticulum cell, or the acute nonlipoid-storing phase, is in the case of the infant who develops a rapidly progressing disease characterized by multiple skeletal lesions, proptosis and visceral involvement, with early and quickly spreading cutaneous manifestations accompanied occasionally by diabetes insipidus, by profound anemia and by high mortality. The pathological picture by biopsy of the various tissues involved will usually reveal a widespread reticulum cell growth with occasional xanthoma cells in which there is no evidence of lipid storage. This stage will vary frequently and fuse almost imperceptibly with the subacute xanthomatous stage of Hand-Schüller-Christian type. Here the skin lesions will be less noticeable. There will be little, if any, visceral involvement, and the diabetes insipidus will be easily controllable in the vast majority of cases by the use of posterior pituitary extract and radiation of the sella. The skull lesions — all of which are identical in all three phases of the disease — will respond rather quickly to X-ray therapy. The response to X-ray therapy in the Letterer-Siwe type, or reticulum cell type, is usually poor.

The final chronic stage, that of "eosinophilic granuloma," is characterized most usually by monolocular lesions, but they may be skeletal as well as calvarial. The lesions will respond quickly to either surgery or X-ray; many patients have had uneventful recoveries by surgical curettage alone. Diabetes insipidus is usually not demonstrable, and skin lesions are

only occasionally met with. The patient, while prone to recurrences in other parts of the skeletal system, usually makes an uneventful recovery following either surgical or deep X-ray therapy.

From the Roentgenographic diagnostic standpoint, there is practically no difference between the three phases, illustrating again the unity of the clinicopathologic picture. Thus Caffey states: "In the skeleton, the radiolucent granulomatous proliferations replace radiopaque bone and appear Roentgenographically as areas of diminished density in the flat bones of the skull, pelvis and shoulder girdle, and also in the tubular bones of the thorax and extremities. Involvement of the bones distal to the elbows and knees is practically unknown. These bony defects may be single or multiple; they are usually sharply demarcated and rounded or scalloped, and are of variable size.

"In cholesterol reticulosis (Schüller-Christian's disease and Letterer-Siwe's disease) the Roentgenographic findings are identical."

Under "eosinophilic granuloma," Caffey states: "Roentgenographically, the skeletal changes are identical with those of cholesterol reticulosis."

DIFFERENTIAL DIAGNOSIS.

A differential diagnosis on these patients must be made first from the standpoint of the skull lesions. The skull lesions are frequently confused with those of multiple myeloma and metastases from carcinoma. Lues and tuberculosis will occasionally produce this type of skull lesion. The outstanding feature in the behavior of this group is their usually quick response to deep X-ray therapy. Large tumor masses will disappear quickly and almost melt away within a question of days following administration of deep X-ray therapy to the calvarium, to the orbit and to the long bones as well.

The second differential diagnosis is the one that concerns the otologist specifically, and that is the differential diagnosis of temporal bone disease. It has been obvious to the writer in his examinations of these patients that the temporal bone lesion is frequently mistaken clinically for cholesteatoma. Indeed, several of these patients described above were originally diagnosed as having attic cholesteatomata. The fetid discharge, the frequent attic perforation, the evidence of bone destruction, conductive deafness and the Roentgen demonstration of trabecular destruction — all fit in very nicely with the diagnosis of cholesteatoma. What confuses the picture still further is that a smear taken for cholesterol crystals will almost always demonstrate them in histiocytic granuloma, particularly of the xanthomatous type, as well as in cholesteatoma. The differential diagnosis is best made by X-raying the skull for other lesions, by making a close search for diabetes insipidus by urine concentration studies, and by careful study of the eyes for evidence of early proptosis. The removal of a bit of granulation tissue for biopsy is an extremely valuable procedure and will frequently make the diagnosis. The response of the temporal bone to X-ray is just as dramatic as is the response to X-ray of the other cranial bones. The otorrhea will frequently cease, and the tympanic perforation will frequently heal entirely, following adequate deep X-ray therapy. The X-ray findings are of no value in distinguishing histiocytic granuloma from cholesteatoma unless a careful study is made of the other cranial bones by X-ray.

TREATMENT.

Inasmuch as the basic etiologic agent for the production of the histiocytic proliferation characteristic of the three phases of histiocytic granuloma is unknown, no specific therapy can be employed at the present time. The proponents of the virus theory have little or nothing in the way of proof for their thesis. The proponents of the hypercholesterolemic type due to increased cholesterol absorption and circulation or poor cholesterol excretion have little or nothing to say in their defense.

In short, we do not know anything at all about the etiology of this interesting type of granuloma; however, it has been observed that in most instances this lesion responds very quickly to deep Roentgen therapy.

The first acute phase of the disease, the reticulum cell type of Letterer-Siwe, usually does not show a good response to deep X-ray therapy. The response may be temporary or partial; but it rarely is of sufficient value to completely control the disease, and the patient usually succumbs to widespread granulomatous lesions which eventually interfere either with pulmonary, hepatic or cerebral function.

The subacute xanthomatous stage of Hand-Schüller-Christian shows a beautiful response to deep X-ray therapy in the vast majority of instances. There are, however, a large number that do not respond.

The third chronic low-grade eosinophilic phase very quickly responds to Roentgen therapy, but is as equally responsive to surgical extirpation. The judgment as to which to employ depends a great deal upon the site of involvement, mechanical factors that have to be considered and size of the lesions. An extremely large lesion might better be treated surgically with radiation reserved for the treatment of any residual swellings or recurrences.

Due to the limitations of space, it is impossible to report in detail on each of the 18 cases. The 18 cases are summarized in the chart at the end of the paper. The following three cases are somewhat typical and illustrate the main features of the disease.

CASE REPORTS.

Case 1. S. W.

History: This boy was first admitted to Children's Hospital on Feb. 16, 1944, at the age of two years, with a history of a chronic draining right ear of four months' duration, which had appeared spontaneously following a mild upper respiratory infection. The discharge was offensive and watery since onset. For the past month before admission, there had been a progressively increasing swelling in the right preauricular area.

Findings: Examination on admission revealed an unusually foul, profuse right otorrhea. The odor was foul but distinctly different from that noticed in cholesteatoma. The right external auditory canal was com-

pletely filled with a gray, friable, vascular mass. The tympanic membrane could not be seen. There was marked sagging of the superior canal wall. There was a large preauricular soft swelling which extended over the zygoma and obliterated the superior aspect of the postauricular crease. There were no other significant findings on physical examination. X-ray studies at that time showed equivocal findings in the right mastoid. Culture from the ear discharge revealed no growth of bacteria or fungi. Biopsy of a polypoid mass removed from the canal was reported as being too indefinite for a diagnosis.

Course: Because of the marked swelling and discharge, it was decided to perform an exploratory mastoidectomy on the right ear. Accordingly, on Feb. 19, 1944, a postauricular approach was made to the right mastoid; a large tumor mass was found to involve the entire temporal bone on the right side with complete necrosis of all mastoid cellular structure and complete exposure of the dura and the lateral sinus. The squama was almost entirely gone. A large defect extended posteriorly into the occipital bone and posteromedially toward the petron itself. Nowhere did the mass appear to encroach upon either the middle ear or the tympanic membrane. The superior and posterior bony canal walls were completely gone. The bulk of the tumor mass and necrotic bone areas was removed. The wound was closed with a T-flap, following the classical method of a radical mastoidectomy; however, no exenteration was performed in the tympanum inasmuch as it appeared to be uninvolved.

The material was distinctly different from the gross appearance of either a primary or secondary cholesteatoma; it resembled tumor tissue and had a very foul odor, differing markedly from the foul odor of cholesteatoma. Following surgery, a moderate otorrhea persisted. Histological sections were studied at length by the pathologist, who was unable to come to a definite diagnosis. His report read in part: "There appears to be some spaces which are lined with low keloidal type cells but they are indefinite, due to the presence of numbers of cells of large mononuclear or plasma cell type. In addition, occasional giant cells are scattered about. These for the most part are elongated, are relatively small, and have from six to 10 nuclei in them. The nuclei are somewhat elongated. Very few giant cells are noted which have round nuclei. On the margins of some of the necrotic areas some fibroblasts can be seen and there is a very definite inflammatory reaction in the form of occasional polymorphonuclears, some plasma cells and some large mononuclear cells; occasionally some eosinophiles are noted." The pathologist, upon further study, stated as follows: "This bears more of the aspect of tumor tissue than that of a chronic granulomatous reaction."

Because of the lack of adequate response to surgery and persistent otorrhea, deep X-ray therapy was started empirically with no definite diagnosis. Patient was discharged from the hospital and followed on the outside by a pediatrician, as well as by the author.

In July, 1944, approximately five months following his discharge from the hospital, his mother noted that he suddenly began to crave large quantities of fluids. This continued until his next admission to the hospital in October, 1944. He drank huge quantities of water and urinated 20 to 25 times daily. In August, 1944, his appetite became poor and he began to lose weight. On readmission, the only positive findings were a healed right mastoid wound with a normal tympanic membrane and a large, widened and deformed external auditory canal. The specific gravity of the urine was 1.003; the blood plasma cholesterol value was 229 mg.

per cent. Further X-rays of the skull revealed an extensive defect consistent with xanthomatosis, involving the floor of the middle fossa. It was the impression that he had very definite diabetes insipidus, and further X-ray therapy to the pituitary region was advised. He was then discharged from the hospital and followed as an outpatient. He has been seen regularly by the writer since that date and was recently examined in September, 1948. During the past four years he has maintained excellent nutrition. His diabetes insipidus was controlled after about four months of Roentgen therapy to the sella turcica region. During these four years, however, he has had at least six episodes of painless swelling in the right parietal, temporal and occipital areas. He has had several areas of regrowth of redundant granulomatous tissue into the external auditory canal. Each episode of swelling of the skull was immediately followed by one or two suberythema doses of deep Roentgen therapy. In every episode so far during the last four years each mass has disappeared.

A biopsy of a piece of tissue removed in July, 1947, was described histologically as follows: "The specimen is made up of a loose network of fine connective tissue; in this are infiltrated numerous inflammatory cells of all types. In some areas, polymorphonuclears predominate; in other areas, numerous eosinophiles are present. There are also lymphocytes, plasma cells, eosinophilic plasma cells. In one margin of tissue there are some quite large cells which have foamy cytoplasm in abundance. The cytoplasm appears to be vacuolated. Occasional mononuclear cells are

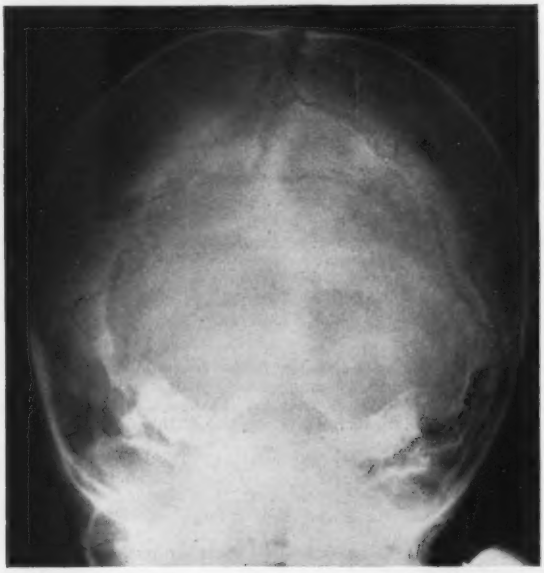


Fig. 1. Case 1. S. W. Posteroanterior view of skull showing extensive lesion in the right temporal bone with replacement of all of the pneumatized area by granuloma.

present. The foam cells are consistent with cells seen in xanthoma. These are large mononuclear phagocytic cells which have picked up fat."

Discussion: This patient has now been followed for almost five years. He presented two findings, chronic otorrhea due to mastoiditis and diabetes insipidus. He had no proptosis and no other significant findings. A great deal of difficulty was encountered in making a pathological diagnosis because of the great variation in histological structure in the specimens examined; however, in retrospect, it is easy to see how one could have made a diagnosis either of the subacute stage of histiocytic granuloma (Hand-Schüller-Christian's disease) or eosinophilic granuloma, the chronic stage. As noted above, sections revealed not only typical reticuloendothelial formations but large clumps of eosinophiles and large groups of xanthoma, or foam cells; however, in view of the clinical findings of diabetes insipidus and a huge temporal bone lesion followed later by local multiple recurrences, it is obvious that this case does not fit into the chronic, or eosinophilic granuloma, pattern but rather into the subacute, or Hand-Schüller-Christian, pattern of histiocytic granuloma.

Case 2. W. E.

History: This patient was first admitted to Children's Hospital on Sept. 16, 1936, at the age of two years and four months. In March, 1936, when he was less than two years old, he received an injury to the left orbit, following which the eye became prominent and red.

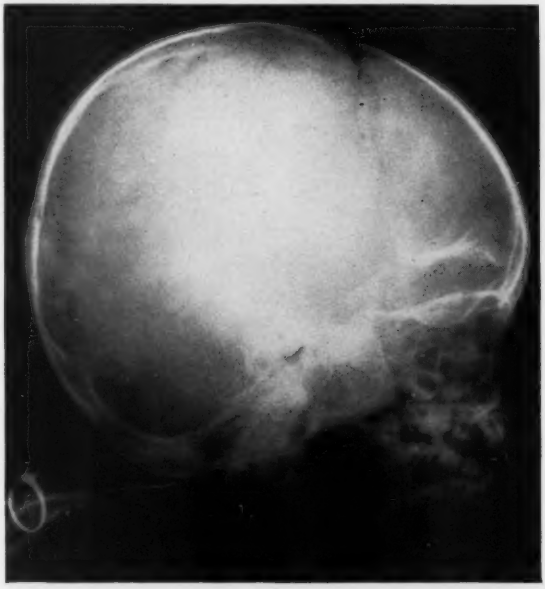


Fig. 2. Case 2. W. E. Patient on admission shows a very slight beginning skull lesion.

Findings: Examination at that time revealed a marked proptosis of the left eye with a widened palpebral fissure. There were no other abnormal findings. There was a slight swelling of the lateral margin of the orbit, and the bony lateral orbital wall could not be palpated. X-ray at that time revealed a destruction of the outer rim of the left orbit, apparently from pressure. The orbit was enlarged.

Course: An exploration of the left orbit was performed. Some of the abnormal tissue in the orbit was sent for biopsy. The report by the pathologist contained the following statements: "There are many polyhedral and round tumor cells within the vesicular nuclei and pink staining cytoplasm. There are also many large cells which contain pigment giving a positive test for iron. There are also a number of giant cells containing from two to six or eight nuclei. A few of these, at least, are typical foreign body giant cells." There were many other remarks indicating real difficulty in establishing a real pathological diagnosis and the final statement was, "Tumor tissue, moderately malignant, type of primary site unknown."

The patient was then discharged from the hospital and X-ray therapy was advised. He was definitely improved on X-ray therapy and continued in good general health. He was, however, readmitted to the hospital on Aug. 9, 1937, for further study because of a beginning fullness in the right temporal fossa. In view of the appearance of a new skull lesion, further X-rays were done, and these showed beginning erosion in the outer right orbit plus several eroded areas in other parts of the skull. At this time, the Roentgenologist suspected that we were dealing with xanthomatosis.

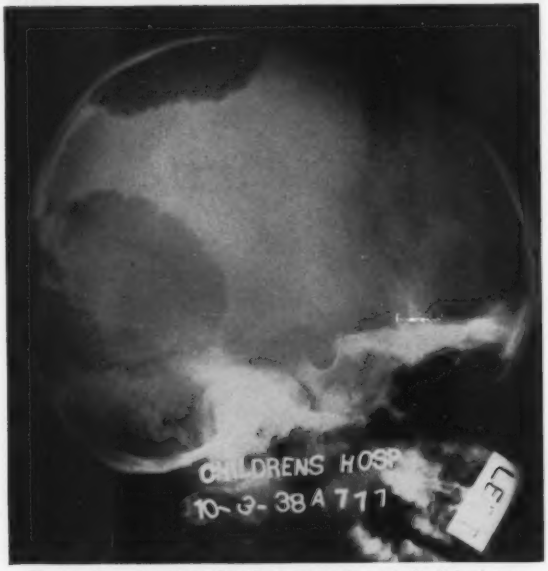


Fig. 3. Case 2. W. E. Marked extension of skull lesions.

During this hospitalization for study, a request was made for otolaryngologic consultation, since neither tympanic membrane could be visualized because of debris and cerumen. The writer saw the patient on Aug. 21, 1937, for the first time. Examination at that time revealed the following findings: The left ear canal contained a peculiar type of granulation tissue which obstructed a view of the left tympanic membrane. The right tympanic membrane was visualized and was perfectly normal in every way. Within two days of observation, the granulation tissue noted in the left ear increased greatly and appeared to be actually polypoid. These polypoid granulations were then removed and at time of surgery were noted to be of intratympanic origin. Foul purulent discharge was noted following removal of the polypoid granulation tissue. The report of the pathologist on the biopsy of these polypoid areas was that of definite xanthomatosis. "The specimen consists of bits of tissue, the typical cells of which are large, pale, foamy cells having vesicu'ar nuclei. Many of these cells are multinucleated and show vacuoles in their cytoplasm. Numerous acute inflammatory cells including polymorphonuclears, lymphocytes and plasma cells are found infiltrating the area occupied by the large cells and forming a marginal false membrane about the greater part of the section. The remaining portion of the periphery is covered by a small piece of degenerated squamous epithelium. Diagnosis—Xanthomatosis."

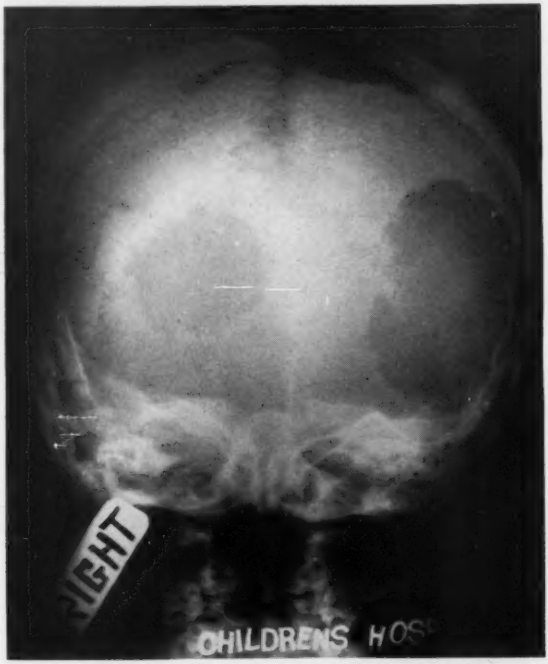


Fig. 4. Case 2. W. E. Further extension of skull lesions.

In view of these otologic biopsy findings, it was believed that perhaps the entire lesion was that of Hand-Schüller-Christian's disease and that the lesion previously considered tumor of the orbit was truly xanthomatosis. Accordingly, deep X-ray therapy was ordered to the left temporal bone area. During the patient's stay in the hospital for observation and X-ray therapy, the otological examinations were repeated practically daily. As noted above, the right tympanic membrane, when first examined on Aug. 26, 1937, was perfectly normal; however, on Oct. 15, 1937, approximately seven weeks later, a definite change was noted in the right tympanic membrane. A yellow color appeared over the region of the promontory as seen through the tympanic membrane, and within a day or two it was obvious that we were dealing with a yellow type of tissue, nonfluid, growing within the right tympanum. At that time the patient was discharged to be followed in the outpatient clinic.

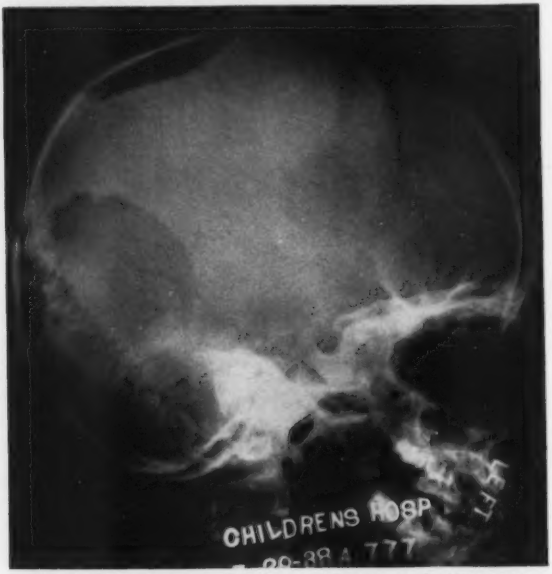


Fig. 5. Case 2. W. E. Further extension of skull lesions.

Observation of both ears was maintained. The left ear continued to discharge profusely in spite of intensive deep X-ray therapy; cultures were consistently negative. The right tympanic membrane continued to have a yellowish discoloration until Feb. 5, 1938, when a beginning bulge appeared in the posterosuperior quadrant. This bulging area persisted until May 4, 1948, at which time, for the first time, a moderately profuse spontaneous otorrhea appeared on the right side. Within three days the entire right tympanic membrane was obscured by polypoid granuloma almost identical grossly with that noted in the left ear. Accordingly, X-ray therapy was advised for the right ear as well, and on Sept. 9, 1938, both tympanic membranes were perfectly dry and healed as a result of such therapy.

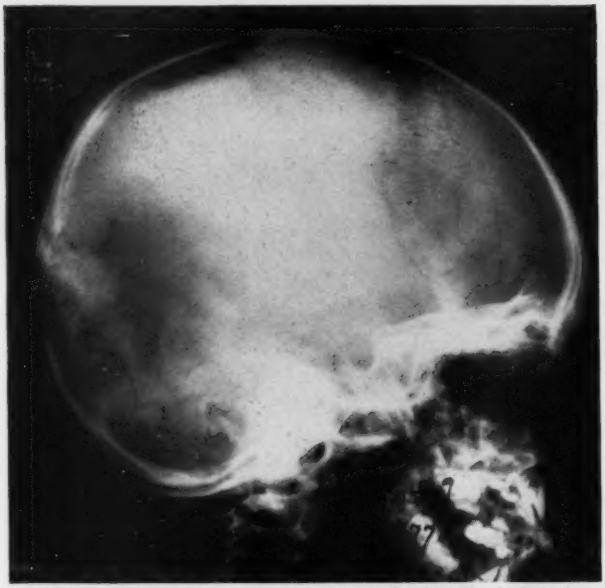


Fig. 6. Case 2. W. E. Note improvement and healing in skull lesions following deep X-ray therapy.

The child continued to improve in general; the proptoses disappeared almost entirely; there were no skin lesions, and the patient was able to be up and about and carry on very well in school. In February, 1939, the mother noted that he began to urinate frequently and to show great thirst; so he was admitted for further study. A diagnosis was made at that time of diabetes insipidus due to pituitary involvement by the xanthomatous process. He was referred back to the Roentgenologist for deep therapy to the pituitary region. He was treated in the outpatient department with pitressin and his daily output was not too great, varying from 1,000 to 1,500 cc.; the specific gravity of the urine varied from 1.003 to 1.013. His general condition remained quite good. He was in school and was quite active. There were no gross temporal bone or frontal bone lesions. His diabetes insipidus was fairly well controlled from 1939 to 1942, and both ears remained dry; however, on Nov. 25, 1942, he was readmitted due to a sudden onset of convulsions and anuria, and became rapidly worse. The neurologist felt that he had a hypothalamic pressure syndrome. A marked hyperpyrexia appeared, and the patient expired on Dec. 9, 1942.

Autopsy: Excerpt of autopsy report by Dr. Ralph Knutti is as follows: "The skull is distinctly thinned out and averages at the line of incision, which does not include the flattened area described above, about 2 mm. in thickness. It is, however, extremely hard and difficult to saw. There is no definite line of demarcation between the inner and outer tables. When the calvarium is removed the flattened area at the vertex shows a

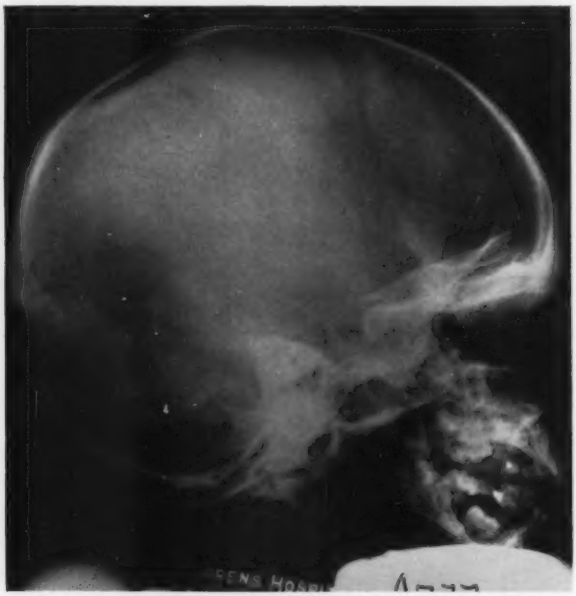


Fig. 7. Case 2. W. E. Skull lesions have almost completely filled in. X-ray taken one month before death.

complete absence of bony structure at its center. In a round area measuring about 1.3 cm. in diameter, very thin bone then appears and this gradually increases in thickness until it reaches the margin of the area. In the flat spot in the temporo-occipital region there is bone covering the entire area, but it is thinned down to 1 mm. in thickness. There is no evidence of yellow discoloration at any of these sites. When the calvarium is removed and the dura is incised, the brain is exposed and it shows marked subarachnoid edema. Brain is rather tense. Coronal sections of brain show no evidence of dilatation of ventricles. *On sections through the medulla, however, there are irregular circumscribed yellowish areas.*

"About the sella there is distinct yellow discoloration to the bone; and when the sella is chiseled away to remove the pituitary, there are yellow foci both in the bone and in the dura about the pituitary. When the middle and inner ears are opened, no exudate is noted; but there are distinct brilliant yellow foci in the bone on both sides. This is more marked on the left.

"The pituitary itself is not remarkable. About it, however, and the underlying skull and in the dura about it, there are numerous large, pale, foamy-appearing cells which are so numerous in the connective tissue that it seems to be much thicker than normal dura, and the cells are also infiltrated into the periosteum. The bone itself shows no distinctive

1.	Name	1. R.E. M	2. S.W. M	3. W.E. M
2.	Hospital	CH	CH	CH
3.	Hospital No.	29-3057	44-3889	36-2929
4.	Age of onset	3 years	20 months	23 months
5.	Duration of observation	19 years	4½ years	6½ years
6.	Outcome—alive or dead. Age.	Alive and well—age 22	Alive and well—age 6	Died—age 8½
7.	SKULL LESIONS Frontal	X	O	X
8.	Temporal with otorrhea	O	X	X
9.	Temporal without otorrhea	X		
10.	Parietal	X	X	X
11.	Occipital	X	O	X
12.	Orbit	X	O	X
13.	Sella	O	X	X
14.	Proptosis	X	O	X
15.	Diabetes insipidus	X	X	X
16.	Skeletal lesions	X pelvis	O	O
17.	Skin lesions	O	O	O
18.	Visceral lesions	O	O	O
19.	Abnormal lab. findings	O	Cholesterol—227 mgm. % Urine sp. gr. 1.003	Urine sp. gr. 1.003
20.	Miscellaneous findings	O	O	Central nervous system disease
21.	Surgery	O	Modified radical mastoidectomy	Orbital decompression polypectomy aural
22.	Radiation	X	X	X
23.	Histological findings	O	Eosinophilia, xanthoma and chronic granuloma	Xanthomatous granuloma
24.	Pathologist's diagnosis	O	Xanthomatosis	Xanthomatosis
25.	Comment	1st clinical diagnosis: Multiple myeloma	1st pathological diagnosis: "tumor" 2nd: Xanthomatosis	1st pathological diag.: "malignant tumor" 2nd: Xanthomatosis

	4. C.B. F	5. L.V. M	6. P.L. M	7. D.T. F	8. J.A. F
	CH	CH	CH	CH	CH
	44-2633	43-3684	41-723	43-3323	962
	27 months	11 years	3 years	6 months	2½ years
	4 years	5 years	4½ years	2 years	2 years
	Alive and well—age 6	Alive and well—age 16	Alive—age 7½ years	Alive?	Alive?
	O	X	X	X	X
	X	O	X	X	X
	O	O			
	X	O	X	X	O
	O	O	X	X	X
	O	O	X	X	X
	O	O	X	?	?
	O	O	X	X	X
	X	O	O	X	O
	O	O	X hip, etc.	O	X Shoulder,
	O	O	X—petechiae, generalized	X—petechial and seborrheic rash	X
	O	O	X Liver, spleen	X Liver, spleen	O
003	Urine sp. gr.1.004 Cholesterol 220	O	O	Urine sp. gr. 1.008	O
ıs	O	O	Sepsis, marked	O	O
pression ural	O	Surgical curettage Frontal bone lesion	O	O	Occipital t removed
	X	O	X	X	X
granuloma	O	Xanthoma	O	O	Xanthoma
s	O	Xanthoma	O	O	Xanthoma
l diag.: mor" atosis	Clinical diagnosis: H.S.C.	Xanthoma solitary lesion	Xanthomatosis	Xanthomatosis	Xanthoma

A. F	9. S.S. F	10. D.K M	11. E.M. F	12. R.S. M	13. E.M. F	14. P.M. M
	CH	CH	CH	CH	CH	CH
	46-3373	2207	4616	18353	37-80	36-1931
ears	11 months	2 years and 4 months	15 months	9	2 years and 10 months	2 years and 5 months
rs	1 week	2½ years	6 months	3 months	1 month	3 weeks
?	Died—age 3½	Alive and well	Died	Alive	Alive?	?
	X	O	X	O	O	X
	X	O	X	O	O	?
		X		O	O	X
	X	X	X	O	X	X
	X	O	X	O	O	X
	X	O	O	X	O	X
	X	O	O	O	O	X
	X	O	O	O	O	X
	X	O	O	O	O	O
lder, pelvis	X	O	O	O	X—humerus, femur	X—femur
	X	O	X	O	O	O
	X	O	X Liver, spleen	O	O	O
	O	O	Anemia, purpura	O	O	O
	O	O	Cervical adenitis	O	O	O
ital tumor ved	Mastoidectomy	Removal of skull tumor (parietal)	Aural polypectomy	Aspiration	O	O
	X	X	X	Just starting	O	O
homa	Xanthomatosis	Reticulum and foam cells and eosinophiles	Reticulum and foam cells	Eosinophilic infiltration	O	O
homa	Xanthomatosis H.S.C.	O	L-S disease	Eosinophilic granuloma	O	O
homa	Letterer-Siwe Xanthomatosis	Could be calle ! . ither E.G. or Xanthomatosis, or even Letterer-Siwe	Diagnosis: L-S disease		Diagnosis: Probable ?Xanthoma	Diagnosis: ? anthoma

12. R.S. M	13. E.M. F	14. P.M. M	15. E.R. F	16. V.G. M	17. G.P. M	18.
CH	CH	CH	L.A.C.H.	L.A.C.H.	L.A.C.H.	L.A.C
18353	37-80	36-1931	1089-022	824-548	957-041	483-7
9	2 years and 10 months	2 years and 5 months	7 months	25 years	35 years	3 yea
3 months	1 month	3 weeks	4 months	16 years	12 years	4 yea
Alive	Alive?	?	Dead— 11 months	Dead— 41 years	Alive	Alive
O	O	X	O	O	X	X
O	O	?	Bilateral	O	O	O
O	O	X		O	O	X
O	X	X	O	O	O	X
O	O	X	O	O	O	O
X	O	X	O	O	X	X
O	O	X	O	X	O	O
O	O	X	O	O	X	X
O	O	O	O	X	O	O
O	X—humerus, femur	X—femur	O	Numerous long bones	O	Mano
O	O	O	Marked, especially on skull	O	O	O
O	O	O	Liver, spleen, icterus, ascites	Prob. myocardial involvement	O	O
O	O	O	Icterus index—42	Blood cholesterol— 133 mgm. %	O	O
O	O	O	Petechiae, diffuse	O	O	Many teeth
Aspiration	O	O	Mastoidectomy	Removal ilium cyst	Removal frontal bone lesion	Dent extra
Just starting	O	O	Temporal bones	X	X	X
Eosinophilic infiltration	O	O	Histiocytosis	Reticulum cells, eosinophiles, xanthoma cells	Eosinophiles and monocytes	O
Eosinophilic granuloma	O	O	Eosinophilic granuloma	Hand-Schuller-Christian's	Eosinophilic granuloma	O
	Diagnosis: Probable ?Xanthoma	Diagnosis: ? anthoma	Pediatric diagnosis: Letterer-Siwe dis.	Was most likely an eosinophilic granuloma	O	X-ray Hand Chris

18. J.S. M
L.A.C.H.
183-797
3 years
4 years
Alive
X
O
X
X
O
X
O
X
O
Mandible
O
O
O
Many loose teeth
Dental extractions
X
O
O
X-ray diagnosis: Hand-Schuller-Christian's dis.

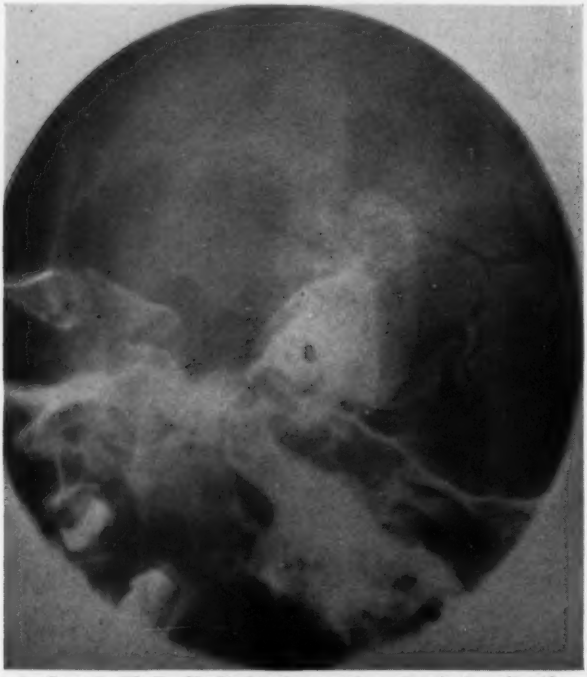


Fig. 8. Case 2. W. E. Skull showing erosion of anterior clinoid process of sella turcica and showing lesion in temporal bone.

abnormality; the bone marrow, although scanty, is negative. Other sections of skull show evidence of bone atrophy, and in many of the bony spaces there are numerous large foam cells similar to those described above. These areas of foam cell infiltration correspond to the areas of yellow discoloration described in the gross.

Discussion: This patient was followed for six years. He gave the clinical findings of bilateral proptosis, bilateral temporal bone lesions, diabetes insipidus, widespread generalized skull lesions, and terminal cerebral involvement. In view of his more or less chronic course, he must be considered to be a subacute fatal form of histiocytic granuloma in which death resulted from cerebral involvement even though all of the skull lesions and diabetes insipidus were completely cleared following deep X-ray therapy. The final impression, therefore, is that we were dealing here with subacute histiocytic granuloma of the xanthomatous type falling most readily into the Hand-Schüller-Christian designation.

Case 3. S. S.

History: This three-year-old white female was admitted to Children's Hospital on Aug. 30, 1946, with the following history: At the age of

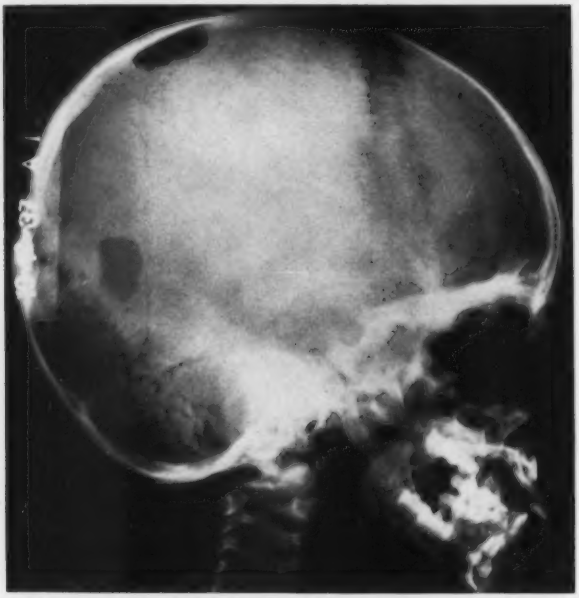


Fig. 9. Case 2. W. E. Lateral view of skull showing progression of parietal and occipital lesions.

11 months, in July, 1944, the child developed spontaneous bilateral draining ears which did not follow either upper respiratory infection or contagious disease. At the same time, the skin over her chest and under her right arm became raw and started to drain serous fluid. This clinical picture persisted until November, 1944, when she developed a lump over the right forehead, which increased in size over a period of several weeks. It was incised by a local doctor, but did not clear up. At about this time, the skin lesions which had started several months before had become larger, so that they now spread to involve the entire body and scalp. The lesions were crusted and were occasionally weeping. At this time a diagnosis of probable xanthomatosis was made, and she received X-ray therapy for the tumor of the skull, the mastoiditis, and the skin lesions. Because of the continuation of the otorrhea, in November, 1945, a bilateral simple mastoidectomy was performed elsewhere. The ears, however, continued to drain in spite of the fact that the mastoid wounds healed nicely. X-ray therapy was continued to the skin and the scalp lesions. Following surgery to the mastoid regions, the child began to drink constantly and urinated profusely. She was then treated with posterior pituitary powder by insufflation, with some improvement; however, from that time until July, 1946, her course was progressively downhill. The skin lesions became more advanced, the tumors of the scalp became greater, and the diabetes insipidus persisted. In July, 1946, jaundice appeared, and the child was then noted to have diarrhea with-

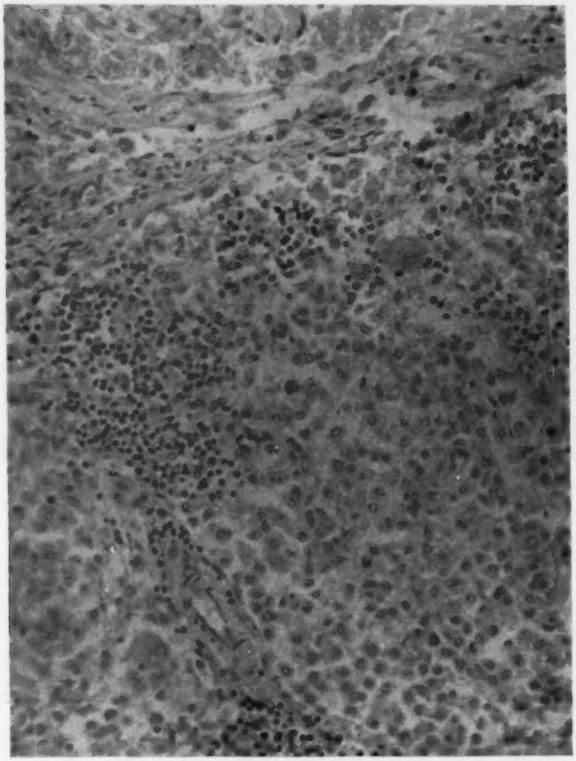


Fig. 10. Case 2. W. E. Section of base of skull in hypophyseal area showing large accumulation of pale xanthoma, or foam, cells characteristic of subacute histiocytic granuloma (Hand-Schüller-Christian's disease).

out blood. Her urine became dark about this time, and the eyes became rather prominent. A protrusion of the abdomen was also noted, and her general condition became poor.

Findings: On admission the child appeared to be in great distress. The temperature was 99.8°, pulse 120, respirations 28. The body weight was 24¾ pounds (the normal for that age and height should have been 31 pounds). The height was 35½ inches (the normal for her age was 36½ inches). She appeared to be an emaciated, chronically ill, white female of three years. Examination of the head revealed a defect in the right frontal area, which was soft to palpation. It measured 2 x 2 cm. A similar defect was noted over the left parietal area, which measured 2 x 2 cm. and was tender. There was a slight left exophthalmos; both sclerae were markedly icteric. Both ear canals were filled with a foul seromucoid discharge; a marked crusting skin lesion obscured both

postauricular mastoid scars. There were crusts of both anterior nares. The liver was easily outlined through the wall, and it filled the entire whole right upper quadrant. The skin was markedly icteric and was covered from head to toe with crusted hemorrhagic lesions. The newer lesions appeared to be purpuric in character.

Laboratory examination at that time revealed a hemoglobin of 49 per cent (7.7 gm.) and 2.8 million red cells. The icterus index was 20. The urine was straw-colored and had a specific gravity of 1.01. X-rays of the entire body at that time revealed lesions resembling those of xanthomatosis or Letterer-Siwe's disease of the skull, scapulae, left clavicle, pelvis, femor and humeri. There was infiltration throughout both lung fields. X-rays of the mastoids revealed marked involvement of both sides.

Course: The child's course in the hospital was rapidly and steadily downhill. She had bouts of fever to 103°, and on the seventh day became markedly dyspneic. Oxygen did not give her any relief. A bone marrow aspiration was done, revealing vacuolated monocytes. The patient died of respiratory distress on Sept. 8, 1946.

Autopsy: Autopsy was done by Dr. Philip Sturgeon. Anatomical diagnoses: *1.* Hand-Schüller-Christian's disease; *2.* deposition of lipoid cells—lung, liver, skull, pituitary, skin; *3.* pulmonary fibrosis; *4.* biliary cirrhosis; *5.* generalized lymphadenopathy; *6.* focal erosions of the skull; 7. double ureter, right; *8* acute bronchopneumonia; *9.* jaundice.

The autopsy notes state as follows: "The brain was opened in the routine manner. On palpation, several large, soft, punched-out defects were felt through the scalp. When the scalp was removed, the defects were identified in the calvarium. The calvarium was removed in the usual manner. The dural surface showed several large defects; however, there were considerably more smaller defects, 1 cm. in diameter, noted externally than were noted on the dural surface. The tissue of the circumscribed areas had a soft, yellow, doughy character. It was estimated that approximately 50 per cent of the calvarium was eroded in this process. The largest defects were 3 to 5 cm. in diameter. Essentially no changes were noted in the arachnoid. The cerebral convolutions and sulci were of average width and depth. There was no injection of the subarachnoid vessels. Anterior fossa had defects similar to those noted in the calvarium. Two such areas, approximately 3 cm. in diameter, were noted over the roof of both orbits. The entire bone surrounding the pituitary was soft and, on sectioning, had a yellow color; however, the anterior and posterior clinoid and adjoining bone were not eroded. On removing the pituitary, some yellow tenacious material was noted over the posterior surface. Both temporal bones were removed; the left could be removed by cutting with a knife almost entirely; the right had to be chiseled in some of its areas. These bones were to be examined by the E. N. T. department."

Among the microscopic findings there were the following quotations: Lungs: "The great bulk of the tissue is made up of thickened septa. These are composed of young fibrous tissue fibroblasts, a few lymphocytes, plasma cells, polymorphonuclears, and a much rarer large cell with a foamy pink cytoplasm. In the lumina are mostly large mononuclear cells with pink homogenous cytoplasm; some have a foamy cytoplasm."

Spleen: "The sinusoids are lined by rather prominent lining cells with large oval nuclei. Several polymorphonuclears and lymphocytes and fre-

Fig. 11. Case 3. S. S. Lateral view of the skull showing marked geographic erosions in the entire skull.

quent eosinophiles are noted in the sinusoids, also some larger mononuclear cells with homogenous pink cytoplasm."

Skull lesions: "On one side there is a wide band of typical foam cells with a few capillaries and little other tissue, then a band of collagenous tissue, next a wide layer of young fibrous tissue and a heavy infiltration of medium-size mononuclear cells with pink homogenous cytoplasm. There is then a band of necrotic cells and another fibrous and mononuclear cell layer. In this last layer there are numerous foam cells, also large mononuclear cells with pink granular cytoplasm. Some of these become quite large and form multinucleated giant cells. In addition, there is a light infiltration with polymorphonuclears and lymphocytes."

Pituitary: "The anterior lobe is identifiable, consisting of acinus-like structures composed of bright red-staining cells, chromophiles, and many purple-staining cells. This ends more or less abruptly in a curving line in a mass of closely packed cells with spindle-shaped nuclei and an abundant narrow, fusiform, irregularly directed cytoplasm. There is one small area of recent hemorrhage into this tissue. A few lymphocytes and a rare polymorphonuclear and eosinophile are noted in this tissue. In some areas there are accumulations of large mononuclear cells with homogenous pink cytoplasm. These are similar to those seen elsewhere A rare foam cell is also present."

Fat analysis by Dr. H. J. Deuel, Jr., Professor of Biochemistry, U. S. C. School of Medicine: "The data show an undoubted increase in the lipid content of the liver and, of course, the characteristic high cholesterol content of the skull. The lipid content of the lungs is also tremendously high along with the cholesterol."

Report of analysis of tissues (results expressed as percentage of dry weight):

Name of Tissue	Dry. Wt. of Aliquots	Lipids %	Free Cholesterol %	Total Cholesterol %	Total Over Free
Liver	0.762	13.8	1.34	1.49	1.11
Skull	0.248	71.9	0.37	16.7	45.2
Kidney	0.546	19.6	0.53	0.9	1.7
Lung	0.986	74.0	0.56	3.45	6.2

Temporal bones were sent by the writer to Dr. Dorothy Wolff, of New York, who very kindly made sections through representative areas of each temporal bone. Examination of these sections revealed the follow-

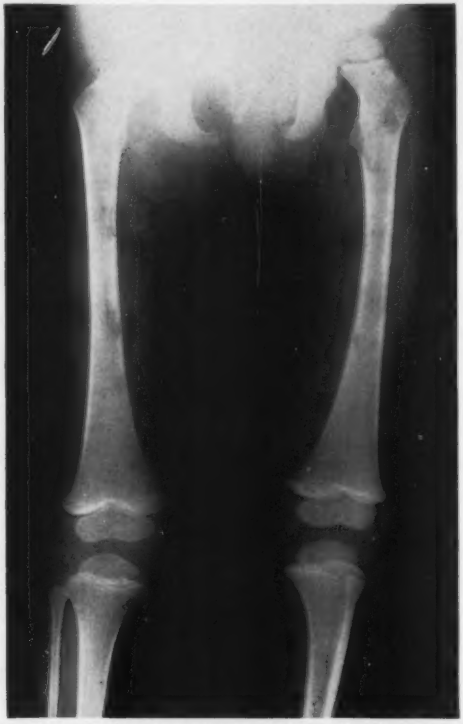


Fig. 12. Case 3, S. S. View showing punched-out lesions in both femurs.

ing findings: There were marked areas of infiltration into all of the pneumatized portions of the temporal bone, including both the mastoid and the petrous portions. These infiltrations were typically granuloma-

tous and contained, in various fields, representations of every phase of histiocytic granuloma. There were numerous areas of marked reticulum cell formation; there were areas of widespread foam cell, or xanthoma cell, formation; and finally there were many areas with large clumps of eosinophiles such as are frequently found in eosinophilic granuloma.

Fig. 13. Case 3. S. S. Temporal bone section showing reticulum cell involvement of pneumatized areas but no involvement anywhere in the scalae. The bony capsule of the labyrinth was apparently able to prevent infiltration of the internal ear by this subacute histiocytic granuloma.

Accordingly, in this one temporal bone it was possible to demonstrate every histological phase of the disease, acute, subacute and chronic, indicating the fact that this was undoubtedly a very severe process which had the opportunity to develop every histologic characteristic of the disease. Interestingly enough, in no section could invasion of the bony capsule of the labyrinth be demonstrated. The cochlea throughout its

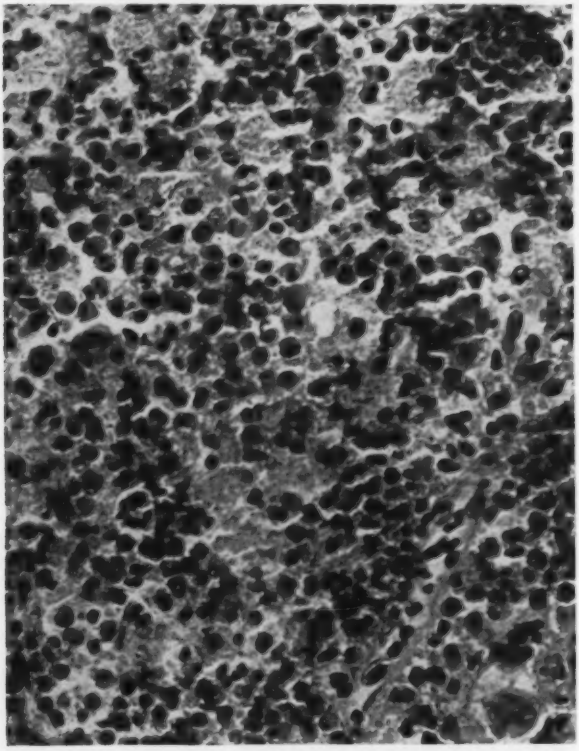


Fig. 14. Case 3. S. S. Section showing numerous eosinophiles, plasma-like cells, histiocytes, and occasional xanthoma-type cells.

coils was essentially normal, as were the various elements of the vestibular apparatus. The infiltration was entirely within the cancellous bone structure and cellular trabeculae of the temporal bones.

Discussion: This case is of great interest in that, first, it showed a fulminating acute process which ended fatally in approximately two years after onset. The disease was characterized by almost every manifestation of histiocytic granuloma, starting with the skin lesion and going on to rapid progression, including skull lesions, proptosis, diabetes insipidus, bilateral temporal bone lesions, hepatomegaly, splenomegaly, icterus, and finally pulmonary involvement. It was possible in this patient to demonstrate all of the histological characteristics of the disease in the acute, subacute and chronic phases. It is also noteworthy

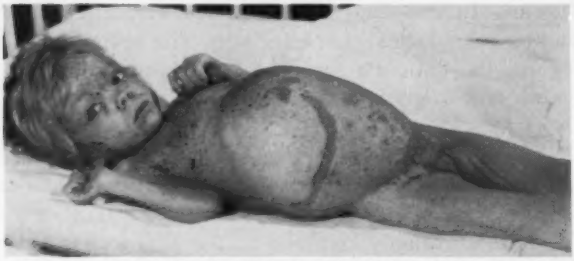


Fig. 15. Case 3. S. S. Photograph showing lateral view of body several days before death. Note the characteristic purpuric seborrheic skin rash over the forehead, scalp, palms, chest and abdomen. Note also the enlarged abdomen, enlarged liver and enlarged spleen as indicated by markings on abdomen.

that response to X-ray therapy and surgery was poor and that, in spite of all treatment, the patient maintained a steady downhill course and finally died.

CONCLUSIONS.

1. Three diseases heretofore considered specific entities, namely, Letterer-Siwe's disease, Hand-Schüller-Christian's disease and eosinophilic granuloma, have been shown by many investigators to be probably different phases of the same basic disease process.

2. The basic disease process is a dysplasia and hyperplasia of the histiocytic or so-called reticuloendothelial system, which creates granulomata which by predilection occur in certain parts of the body. The term "histiocytic granuloma" is proposed as a basic entity to include the three phases.

3. The acute stage of the disease, the reticulum cell type of Letterer-Siwe, is characterized by its occurrence in early infancy; the rapid involvement, not only of the calvarium but of the other skeletal areas; rapid visceral involvement; and early cutaneous manifestations. The mortality is extremely high and the response to treatment by radiation therapy is extremely poor.

4. The subacute, or xanthomatous, stage of Hand-Schüller-Christian's is best typified by the clinical triad of proptosis, skull lesions and diabetes insipidus due to involvement of the

sella turcica. In this stage the xanthoma, or foam cell, is the outstanding pathological characteristic. The prognosis is relatively good, the patient's response to radiation being on the whole quite excellent.

5. The chronic form of the disease characterized by eosinophilia as well as histiocytosis and previously termed eosinophilic granuloma responds equally well to surgery or radiation. It is most usually confined to the long bones but may occur in the calvarium.

6. Eighteen cases are reported for the first time, in many instances showing impossible attempts to categorize the cases into any one of the three phases previously called separate diseases. In most instances, manifestations of two and occasionally of three phases can be found in the same patient.

7. Of statistical interest are the following facts:

a. Of the 18 cases reported, 11 were males and seven females.

b. No "racial" or geographic factors were found to predispose to the disease.

c. Of the 18 cases reported, 11 had temporal bone lesions, 10 with chronic otorrhea.

8. It is important for the otolaryngologist to be highly conscious of the relative frequency of this disease inasmuch as it may very frequently simulate malignant tumors, lues, tuberculosis and other diseases. The patient with an unexplained proptosis, an unexplained diabetes insipidus and a temporal bone lesion of the chronic otorrhea type should be investigated by appropriate Roentgen studies for the possibilities of a histiocytic granuloma.

The response to treatment in this disease, if recognized early, is usually good. Consequently, a plea for early diagnosis must complete these conclusions.

BIBLIOGRAPHY.

1. Abt, A. F., and Denenholz, E. J.: Letterer-Siwe's Disease. *Amer. Jour. Dis. Child.*, 51:499-522, 1936.

2. Bailey, J. W., and Freis, E. D.: Eosinophilic Granuloma of Bone with Manifestations in the Jaw. *Jour. A. D. A.*, 31:91-94, 1944.

3. Bakody, J. T.: Eosinophilic Granuloma of Bone. *Jour. Java State Med. Soc.*, 36:9:397-400, Sept., 1946.

4. Bass, M. H.: Solitary Eosinophilic Granuloma of Bone. *Amer. Jour. Dis. Child.*, 61:6:1254-1262, June, 1941.

5. Behr, Carl: Eye Changes in Schuller-Christian-Hand's Disease. *Arch. f. Ophthal.*, 136:403, 1936.

6. Christian, H. A.: Defects in the Membranous Bones. Exophthalmos and Diabetes Insipidus. Contribution to Medical and Biological Research. New York: Paul B. Hoeber, 1919, 1:390.

7. Coffey, John: Pediatric X-ray Diagnosis. The Year Book Publishers, Inc., 1945, pp. 71-73.

8. Cooper, K. G.: Schuller-Christian's Disease Complicating Mastoiditis. *Rocky Mt. Med. Jour.*, 36:481-484, July, 1939.

9. Curtis, A. C., and Cawley, E. P.: Eosinophilic Granuloma of Bone with Cutaneous Manifestations. *Arch. Derm. and Syph.*, 55:6:810-818, June, 1947.

10. Dauksys, Joseph: Xanthomatosis: Schuller-Christian's Disease. *Med Bull. Vet. Admin.*, 13:40, July, 1936.

11. Druss, J. G.: Aural Manifestations of Lipoid Granulomatosis (Hand-Schuller-Christian's Disease). *Amer. Otol., Rhinol. and Laryngol.*, 45:693-703, 1936.

12. Dundon, C. C.; Williams, H. A., and Laipply, D. C.: Eosinophilic Granuloma of Bone. *Radiology*, 47:5:433-444, Nov., 1946.

13. Engelbreth-Holm, J.; Teilum, G., and Christensen, Erna: Eosinophilic Granuloma of Bone: Schuller-Christian's Disease. *Acta Med. Scandinavica*, 118:292-312, 1944.

14. Farber, Sidney: The Nature of "Solitary or Eosinophilic Granuloma" of Bone. *Amer. Jour. Path.*, 17:14:625-629, July, 1941.

15. Finzi, O.: "Mieloma, etc." *Minerva Med.*, 9:239-241, Feb., 1929.

16. Foot, N. C., and Olcott, C. T.: Non-Lipoid Histiocytosis. *Amer. Jour. Path.*, 10:81-96, 1934.

17. Fraser, John: Skeletal Lipoid Granulomatosis. (Hand-Schuller-Christian's Disease). *Brit. Jour. Surg.*, Vol. XXII, No. 88, 1934-1935, 22:801.

18. Glatt, M. A.: Xanthoma or Lipoid Granuloma of the Temporal Bone (Hand-Schuller-Christian Syndrome). *Arch. Otol.*, 46:2:110-121, Feb., 1946.

19. Green, W. T., and Farber, Sidney: Eosinophilic or Solitary Granuloma of Bone. *Jour. Bone and Joint Surg.*, 24:3:499-526, July, 1942.

20. Gross, P., and Jacox, H. W.: Eosinophilic Granuloma and Certain Other Reticular Endothelial Hyperplasias in Bone. *Amer. Jour. Med. Sci.*, 203:5:673-686, May, 1942.

21. Hamblen, E. C.; Arena, J. M., and Cuyler, W. K.: Hand-Schuller-Christian's Disease. *Amer. Jour. Dis. Child.*, 60:352-358, 1940.

22. Hamilton, J. B.; Barnar, J. L.; Kennedy, P. C., and McCort, J. J.: The Osseus Manifestations of Eosinophilic Granuloma. *Radiology*, 47:445-456, Nov., 1946.

23. Hand, Alfred R.: Polyuria and Tuberculosis. *Arch. Ped.*, 10:673, 1893.

24. Hand, Alfred R.: Defects of Membranous Bones, Exophthalmos and Polyuria in Children: Is It Dyspituitarism? *Amer. Jour. Med. Sci.*, 162:509-515, 1921.

25. Horwitz, Thomas: Eosinophilic Granuloma of the Tibia. *Amer. Jour. Roentgenol. and Rad. Ther.*, 50:3:355-357, Sept., 1943.

26. Imler, Allison S.:, Med. Corps, U. S. Army: Reticuloendotheliosis. (Report of Two Cases.) *Amer. Jour. Roentgenol.*, 56:343, Sept., 1946.

27. Jaffe, Henry L., and Lichtenstein, Louis: Eosinophilic Granuloma of Bone. A Condition Affecting One, Several or Many Bones, But Apparently Limited to the Skeleton, and Representing the Mildest Clinical Expression of the Peculiar Inflammatory Histiocytosis—Also Underlying Letterer-Siwe's Disease and Schuller-Christian's Disease. *Arch. Path.*, 37:99, Feb., 1944.

28. Jaffe, Henry L., and Lichtenstein, Louis: Eosinophilic Granuloma of Bone. *Jour. A. M. A.*, 135:14:935-936, Dec. 6, 1947.

29. Kellogg, Douglas, S.: Xanthomatosis (Lipoidosis. Schuller-Christian Type). Report of a Case. *Amer. Jour. Roentgenol. and Rad. Ther.*, 44:396, Sept., 1940.

30. Kennedy, R. L. J.: Xanthomatosis: Schuller-Christian's Disease. *Proc. Staff Meet., Mayo Clin.*, 13:776-781, Dec. 7, 1938.

31. Kernwein, G. A., and Queen, F. B.: Solitary Eosinophilic Granuloma. *Surg.*, 14:1:105-110, July, 1943.

32. Klotz, Rudolf: Contribution to Schuller-Christian-Hand's Disease (Christian's Syndrome). *Klin. Wchnschr.*, 19:12, Jan. 6, 1940.

33. Lane, Clinton W., and Smith, Margaret G.: LXXIV—Cutaneous Manifestations of Chronic (Idiopathic) Lipoidosis (Hand-Schuller-Christian's Disease): Report of Four Cases, Including Autopsy Observations. *Arch. Dermat. and Syph.*, 39:617, Apr., 1939.

34. Lederer, F. L.; Poncher, H. G., and Fabricant, N. D.: Aural Manifestations of Lipoid Granulomatosis (Xanthomatosis) of the Skull. *Arch. Otol.*, 21:27-40, 1935.

35. Letterer, E.: Aleukamische retikulose. *Frankfurt Ztschr. f. Path.*, 30:377-394, 1924.

36. Lichtenstein, Louis, and Jaffe, H. L.: Eosinophilic Granuloma of Bone with Report of a Case. *Amer. Jour. Path.*, 16:595-604, 1940.

37. Mallory, Tracy B.: Pathology: Diseases of Bone. *N. Eng. Jour. Med.*, 27:25, Part 1, Dec. 17, 1942.

38. Maximow, A. A., and Bloom, W.: Textbook of Histology. W. B. Saunders Co., 1931, pp. 125-126.

39. Michael, P., and Norcross, N. C.: Eosinophilic Granuloma of Bone. *Naval Med. Bull.*, 45:4:661-668, Oct., 1945.

40. Osborne, R. L.; Freis, E. D., and Levin, A. G.: Eosinophilic Granuloma of Bone Presenting Neurologic Signs and Symptoms. *Arch. Neur. and Psych.*, 51:5:452-456, May, 1944.

41. Otani, S., and Ehrlich, J. C.: Solitary Granuloma of Bone (Simulating Primary Neoplasm). *Amer. Jour. Path.*, 16:479-490, 1940.

42. PICK, LUDWIG: A Classification of the Diseases of Lipoid Metabolism and Gaucher's Disease. *Amer. Jour. Med. Sci.*, 185:4:453-469, Apr., 1933.

43. PICK, LUDWIG: Nieman-Pick's Disease and Other Forms of So-called Xanthomatosis. *Amer. Jour. Med. Sci.*, 185:5:601-616, May, 1933.

44. RAAF, JOHN: Eosinophilic Granuloma of the Skull. *West. Jour. Surg., Obst. and Gynec.*, 53:1, Jan., 1945.

45. RILEY, PATRICK: Eosinophilic Granuloma of Bone. *Radiol.*, 47:514-516, Nov., 1946.

46. ROSENWASSER, HENRY: Lipoid Granulomatosis Involving the Middle Ear and Temporal Bone. *Arch. Otol.*, 32:1045-1053, 1940.

47. ROWLAND, RUSSELL S.: Xanthomatosis and the Reticuloendothelial System. *Arch. Int. Med.*, 42:5:611-674, Nov., 1928.

48. SALOMON, M. I., and ENGELSHER, C. L.: Destructive Granuloma of Bone in the Skull. *N. Y. Jour. Med.*, 46:2:183-184, Jan. 15, 1946.

49. SANGUINETTI, CESARE: Ocular Symptoms in the Hand-Schuller-Christian Syndrome (Dysostosis Hypophysaria). *Boll. d'oculistica*, 12:392, Apr., 1933.

50. SCHAIRER, E.: Osteomyelitis mit Eosoniphiler, etc. *Zntrlbl. f. Allg. Path. v. Path. Anat.*, 71:113-117, Nov., 1938.

51. SCHULLER, ARTHUR: Veber Eigenartige Schadeldefekte in Jugendalter. *Ftschr. a. d. geb. d. Roent.*, 23:12, 1915-1916.

52. SHEA, JOHN J. Xanthomatosis (Schuller-Christian's Disease). A Report of a Case with Radiosensitive Pathology in the Mastoid. THE LARYNGOSCOPE, 48:589-598, Aug., 1938.

53. SIWE, S. A.: Die Reticuloendotheliose ein neues Krankheitsbild unter den Hepatosplenomegalien. *Ztschr. f. Kinderh.*, 55:212-247, 1933.

54. SLESINGER, HYMAN A.: Xanthomatosis, Hand-Schuller-Christian's Disease. *Pa. Med. Jour.*, 39:779, July, 1936.

55. SOLOMON, HARRY A., and SCHWARTZ, SHELDON: Eosinophilic Granuloma of Bone. *Jour. A. M. A.*, 128:10:729-731, July 7, 1945.

56. SOSMAN, MERRILL C.: Xanthomatosis. *Jour. A. M. A.*, 98:2:110-117, Jan., 1932.

57. STRAUS, B.: Metabolic and Inflammatory Histiocytosis. *Amer. Jour. Med.*, 5:2:245-252, Aug., 1948.

58. STRONG, ROBERT A.: Xanthomatosis (Schuller-Christian's Disease). *Jour. A. M. A.*, 107:422, Aug. 8, 1936.

59. TEPERSON, HYMAN I.: Xanthomatosis: A Case of Schuller-Christian's Disease Treated by Irradiation. *Radiol.*, 25:440, Oct., 1935.

60. THANNHAUSER, S. J.: Eosinophilic Granuloma of Bone. *Jour. A. M. A.*, 134:16:1437-1438, Aug. 16, 1947.

61. THOMPSON, C. O.; KEEGAN, J. J., and DUNN, A. D.: Defects of Membranous Bones, Exophthalmos and Diabetes Insipidus. Report of a Case with Necropsy. *Arch. Int. Med.*, 36:5:650-666, Nov., 1925.

62. VERSIANI, O.; FIGUEIRO, J. M., and JUNQUEIRA, M. A.: Hand-Schuller-Christian's Syndrome and "Eosinophilic or Solitary Granuloma of Bone." *Amer. Jour. Med. Sci.* (new series), 207:161-166, 1944.

63. WALLGREN, ARVID: Systemic Reticuloendothelial Granuloma (Non-lipoid Reticuloendotheliosis and Schuller-Christian's Disease). *Amer. Jour. Dis. Child.*, 60:3:471-500, Sept., 1940.

64. WEIDMAN, FRED D.: The Eosinophilic Granulomas of the Skin. *Arch. Dermat. and Syph.*, 55:2:155-175, Feb., 1947.

65. WEINSTEIN, A.; FRANCIS, H. C., and SPROFKIN, B. F.: Eosinophilic Granuloma of Bone. *Arch. Int. Med.*, 79:2:176-184, Feb., 1947.

66. WOOD, V. V.: Bilateral Xanthomatosis (Lipoidosis) of the Mastoid: Case Report. *Amer. Otol. Rhinol. and Laryngol.*, 46:991-1008, 1937.

67. WYNKOOP, EDWARD J., and HADLEY, LEE: Schuller-Christian's Disease. Report of a Case. *Arch. Ped.*, 55:417, July, 1938.

NASOPHARYNGEAL IRRADIATION AND HEARING ACUITY: A FOLLOW-UP STUDY OF CHILDREN.*†‡

STACY R. GUILD, Ph.D.,
Baltimore, Md.

My part in this Symposium is to report observations made in a follow-up study of school children. Many persons have participated, at one time or another and in various ways, in the collection of the observations on which this report is based, and I wish at this time specifically to acknowledge this fact and to express my appreciation to all the members, past and present, of the staff of the Department of Otolaryngology who have, by their carefully made hearing tests, good physical examinations, irradiation treatments, etc., made this study possible. Throughout the study I have participated actively in the collection and in the analysis of the observations. This report is based on analyses made mostly by me, and I assume sole responsibility for the content of the report.

The persons whose records form the basis for the present report were first examined in the Otological Research Laboratory of the Johns Hopkins University School of Medicine during the school year 1939-1940, in connection with the study of the hearing of 1365 white school children that was reported at the 1940 meeting of the American Otological Society.[12] During the next two years a large number of the children were re-examined periodically; a report of this two-year follow-up study was made at the 1942 meeting of the Ameri-

*Presented, by invitation, in a Symposium on Irradiation of Lymphoid Tissue in the Nasopharynx, at the Fifty-fourth Annual Session of the American Academy of Ophthalmology and Otolaryngology, Oct. 11, 1949, Chicago, Ill.

†From the Otological Research Laboratory, the Johns Hopkins University School of Medicine.

‡This study was aided by grants to Dr. S. J. Crowe from the John and Mary R. Markle Foundation.

Editor's Note: This ms. received in Laryngoscope Office and accepted for publication, Nov. 21, 1949.

can Otological Society.[9] The shortage of departmental staff incident to the entry of our country into World War II interrupted the program of periodic re-examinations that had been planned. After the war, during 1946 and the first half of 1947, re-examinations were made of all the children, irrespective of whether or not they had been treated, who could then be located and persuaded to return to the laboratory for re-examination. The present report is based on comparisons of the records of the first and of the last examinations made of the children who actually returned in 1946 or 1947.

The shortest interval between the first and the last examinations of the children whose records are used in this report was 6 years, the average interval was slightly over 6½ years. The average age of the children at the time of their first examinations was 9½ years, and at the time of their last examinations slightly over 16 years. The age range at the time of the first examinations was from 8 to 13 years; at the last examination it was from 14 to 21 years.

Selection of the children for examination originally, in 1939-1940, was not on the basis of hearing or of present condition or past history of the nasopharynx or the ears, but was entirely on the basis of enrollment in certain classes of certain schools. The parents of all the children who were then attending regular classes in the third, fourth, fifth or sixth grades of one or another of six Baltimore schools were asked to permit their children to participate in the study. The only departure from a strictly random selection of white children of that age group is therefore the one imposed by the requirement that they be attending regular classes; this automatically excluded certain categories of seriously handicapped children, such as the mentally defective, the blind, the severely crippled, and children with extreme degrees of impaired hearing. The effect on the present report of the exclusion of the latter group will be discussed later.

All examinations were made at the hospital, under suitable conditions for careful work; none was made at a school. All the examiners were well qualified for the parts of the exami-

nations they made. Most of the irradiation treatments were given by Dr. S. J. Crowe personally. The hearing tests, the reliability and accuracy of which particularly concern the credibility of this report, were all made in one or the other of the two "sound-proof" rooms at the laboratory. At each examination, a Western Electric Co. 1-A audiometer was used to determine the thresholds, by air conduction, for tones of 14 frequencies over the range from 32 to 16384 cycles per second; the charts show the frequencies routinely used in the tests. The hearing acuity for spoken voice was also tested at each examination, by means of a W. E. Co. 4-A phonographic audiometer and the two-digit records; and at each examination Weber, Schwabach and Rinne tests were made with a 512 d.v. steel tuning fork. The opposite ear was masked, routinely, during the making of the phonographic, the Schwabach and the Rinne tests; the masking noise was generated in a headphone by a calibrated masking device, locally built, that has been used in the laboratory for many years. Suitable masking was also used, whenever indicated, during the testing with the pure-tone audiometer. The audiometers (two of each kind), the tuning forks and the masking devices were meticulously maintained in proper condition for use throughout the period of time covered by this study. In brief, the last examinations of the children in this study were made under conditions strictly comparable to those that prevailed at the time of the first examinations. This point is stressed because otherwise some of the changes in hearing acuity that occurred might be regarded as apparent rather than as real ones.

CHILDREN WITH GOOD HEARING; NOT TREATED.

The majority of the children examined had good hearing, as would be expected from consideration of the method of selection used. The inclusion of this group in the follow-up study has proved to be important, for three reasons: (1) it has made possible the study of normal ageing changes in hearing acuity during the childhood years; (2) it has provided information with respect to the effect of nasopharyngeal lymphoid tissue on the normal ageing changes that occur

in hearing acuity during childhood; and (3) it has provided a baseline that can be used in the evaluation of the significance of changes that occurred in the hearing acuity of the children who had impairments limited to high tones and who were treated by nasopharyngeal irradiation. It is for the latter reason that the data about this group of untreated children are included in this Symposium on the effects of nasopharyngeal irradiation.

Of the children who returned in 1946 or 1947 for re-examination, a total of 259 met the requirements set up for inclusion in the group in which normal ageing of hearing acuity might be studied; namely, that at the first examination both ears had good hearing or at most a slight impairment for some tones of the very high frequencies, and that during the time between the first and the last examination no treatment of the throat, either irradiative or surgical, was received, either from members of our own organization or from physicians elsewhere. None of the group had had any nasopharyngeal irradiation previous to the first examination, but about half of the children had been submitted to throat surgery, either a tonsillectomy or a tonsillectomy and adenoidectomy, before they entered the study.

The changes in hearing thresholds that occurred in the entire group of 259 children (518 ears) during the period of observation are summarized in Fig. 1. In this, as in all but

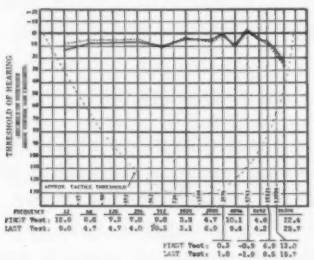


Fig. 1. Normal age changes in hearing acuity during childhood, based on tests of 259 untreated children (518 ears) who were re-examined after six years or longer. As in all except the last figure in this paper, the **solid** line shows the average thresholds of the first audiograms and the dotted line the average thresholds of the last audiogram, and the numerical averages, to the nearest tenth of a decibel, are stated below the chart.

one of the charts used in the report, the audiogram shown by the *solid* line represents the arithmetical averages, or the means, of the air-conduction thresholds for the respective tones at the time of the first examination, and the audiogram shown as a *dotted* line represents the corresponding averages for the last examinations. The actual averages, to the nearest tenth of a decibel, are given in tabular form below each audiogram chart, for the benefit of persons who may care to study the data more exactly than can be done by inspection of the graphic audiograms. It is impossible to show slight differences in thresholds on a standard audiogram form except by using lines so thin that they are not reproduced clearly on the printed page.

Before proceeding to inspect the figures, a few words are in order about the use of averages to present the data of this study. I am well aware of the limitations of the method and of the pitfalls into which averages may lead one when the raw data cover a wide range of variation. For instance, it means nothing to have the average of the ages of the persons in a home for the aged and in a kindergarten class be the same as the average of the ages of the firemen in the city. But when the range of variation for similar items in the raw data is small, the method of averages is satisfactory for most purposes. I believe that to be the case in the present instance; the age range is small, the differences in length of the intervals between the first and last examinations were small compared to the total interval, and the children within each group or subgroup that has been made of the material had only small differences in hearing acuity, compared to the possible range of difference. Certainly this simple method reveals the essential story so well that it has not seemed worth while to use other statistical techniques.

Inspection of the average audiograms displayed in Fig. 1 shows that, for the group of 259 untreated children (518 ears), hearing acuity improved slightly for low tones during the period of observation, became slightly worse for very high tones, and remained almost unchanged for tones of the frequency range from 512 to 8192 cycles per second. The im-

provements for the two lowest tones tested (32 and 64 cycles) were somewhat more than for the lowest tones generally used in audiometric testing, namely, those with the frequencies of 128 and 256 cycles. The reasons for believing that the shifts in thresholds recorded for this group of children represent the normal ageing changes are stated elsewhere in this report.

Only one of the breakdowns that have been, or can be, made of the observations recorded for the group of 259 untreated children, will be presented today. This is the breakdown made on the basis of the recorded appearances of the tubal orifice regions of the nasopharynx, as viewed through a nasopharyngoscope, at the times of the first and of the last examinations, respectively. To avoid the making of subgroups too small to be significant, and at the same time to help avoid confusion in the interpretation of descriptions by different examiners, the classification for each examination has been restricted to two categories: both tubal orifices normal, and one or both tubal orifices abnormal.

The average audiograms for the four subgroups thus made of the 259 untreated children are shown in Fig. 2, parts A to D.

The largest subgroup is the one in which the children had abnormal tubal orifices at the time of the first examination and normal tubal orifices at the time of the last examination. The children, in other words, had had a spontaneous regression of nasopharyngeal lymphoid tissue during the transpubertal period covered by the study. This subgroup consists of 130 children, or almost exactly half of the total group of untreated children. The average audiograms of these 130 children (260 ears) at their first and at their last examinations, which are shown in Fig. 2, A, so closely resemble the corresponding audiograms for the entire group of untreated children, given in Fig. 1, that only by careful inspection and comparison of the two sets of data can even minor differences be noted. I doubt that the minor differences have any significance.

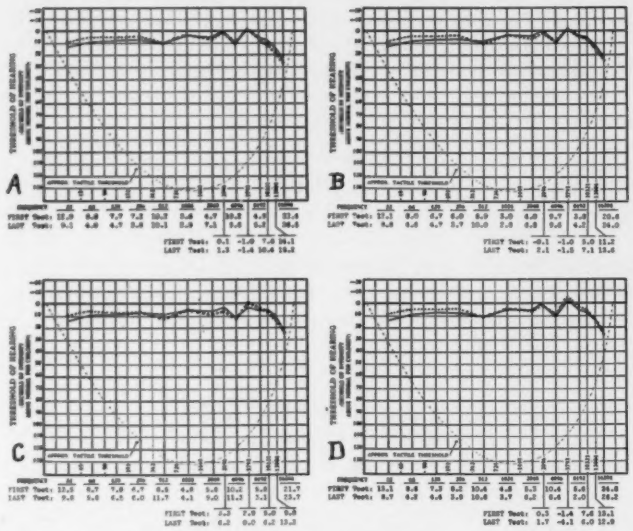


Fig. 2. The average changes in hearing acuity that occurred in each of the four subgroups of the 259 untreated children (see Fig. 1) on the basis of tubal orifice conditions at the times of the first and of the last examinations. See text matter for size of the subgroups, etc.

Sixty-three children, or about one-fourth of the total group of 259 untreated children, had normal appearing tubal orifices at both the first and the last examinations; in other words, they had, probably throughout the entire period of the study, what is usually regarded as the ideal, or the desired, condition of nasopharyngeal lymphoid tissue with respect to its possible effect on hearing acuity. On theoretical grounds it might well be argued that the baseline for normal age changes in hearing acuity of children should be limited to the data for this subgroup. To do so, however, would make no essential difference, as may be seen by comparison of the average audiograms for this subgroup of 63 children (126 ears), shown in Fig. 2, B, with the corresponding data for the children of the entire group (Fig. 1) and with the data for the children whose nasopharyngeal lymphoid tissue in the tubal orifice regions underwent spontaneous regression satisfactorily during the period of observation (Fig. 2, A).

Thirteen of the untreated children who had normal tubal orifices at the first examination had one or both tubal orifices abnormal in appearance, on nasopharyngoscopic inspection, at the time of the last examination; in other words, hyperplasia of lymphoid tissue had developed in the tubal orifice region during the period of the study. The average audiograms for this small subgroup of 13 children (26 ears) are shown in Fig. 2, C. The slight variations from the changes shown in the two preceding subgroups (cf. Fig. 2, A, and Fig. 2, B) are probably due in large part to the small number of cases in this subgroup; certainly the development of lymphoid tissue in the tubal orifice regions did not affect the acuity of hearing for high tones unfavorably.

The average audiograms for the fourth subgroup of the 259 untreated children, made on the basis of tubal orifice conditions, are shown in Fig. 2, D. The subgroup consists of 53 children whose tubal orifices, one or both, were abnormal in appearance at the times of both the first and the last examinations. The shortest interval between the first and the last examinations was 6 years, the average interval was slightly over $6\frac{1}{2}$ years. Presumably an excess amount of lymphoid tissue was present in the tubal orifice region at least most of the time during the interval; this was true for the children who did have intermediate examinations made during the first two years of study. On theoretical grounds these children, who had persistently abnormal tubal orifices for over six years each, should have suffered a greater average loss of hearing acuity than did the children of the subgroups in which spontaneous regression of lymphoid tissue occurred (Fig. 2, A) or in which the tubal orifices were normal throughout the period of observation (Fig. 2, B). Actually, such a loss of thresholds did not occur. Comparison of the data in part D of Fig. 2 with that in parts A and B shows that the gain that occurred in the average thresholds for low tones is strikingly similar to that which occurred in the other two large subgroups, and, most surprising of all, that this is the only one of the subgroups in which a slight loss in acuity of hearing for the very high tones did not occur. I do not

know whether the difference in the changes of thresholds for high tones between this and the other subgroups is statistically significant in the sense of indicating that persistent lymphoid tissue in the tubal orifice region has a beneficial effect on hearing acuity for high tones, but I am certain that the subgroup is large enough — 53 children (106 ears), or slightly over one-fifth of the entire group — that the data prove conclusively that the lymphoid tissue persistently present in the tubal orifice regions of these children for over 6 years did not exert a deleterious effect upon hearing acuity during the period of the study.

CHILDREN WITH IMPAIRED HEARING; TREATED.

With the above data about the untreated children as a background, let us turn now to a consideration of the changes in hearing acuity that occurred in the children who had impaired hearing at the time of their first examinations and who were treated, early in the course of the study, by means of irradiation of nasopharyngeal lymphoid tissue, or by, in a few instances, some combination of throat surgery and nasopharyngeal irradiation, or by, in cases of suppurative otitis media, some form of local non-surgical therapy in addition to irradiation of the nasopharynx.

All the treated children who returned in 1946 or 1947 were among those seen repeatedly during the course of the first two years of the study and whose condition at that time was reported in 1942. In all but ten per cent of the treated children success had been attained in shrinking the nasopharyngeal lymphoid tissue before the end of the two-year period of repeated re-examinations, usually long before.[9] By the time of their return in 1946 or 1947 the treated children, almost without exception, had both tubal orifices entirely normal in appearance, on nasopharyngoscopic inspection. This being the case, the report on the changes in hearing acuity that occurred in them does not have to be complicated by subdivisions of groups on the basis of tubal conditions, but the material can be grouped entirely on the basis of type of hearing impairment present at the time of the first examinations, before treatment was started.

HEARING IMPAIRMENTS LIMITED TO HIGH TONES.

The largest group of the treated children is that in which some form of impairment of hearing for high tones existed, the hearing for low tones being good, usually up to 2048 or higher. The average audiograms for the entire group are presented in Fig. 3. The code is the same as that used in the

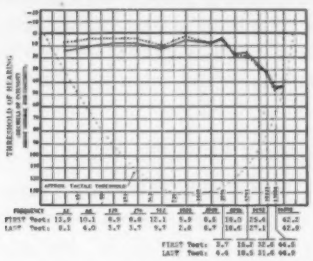


Fig. 3. The averages of the first and of the last audiograms of 95 ears of children who had some form of impaired hearing for high tones and who were treated by nasopharyngeal irradiation. The interval between the tests was six years or longer in each case.

charts about the untreated children (Figs. 1 and 2); the solid line represents the arithmetical averages of the thresholds at the first examination, the dotted line the corresponding data for the last examination. Each of the lines in this chart shows the average of the thresholds of 95 ears. The designation for this group is given as ears, instead of as children, because some of the impairments were unilateral; it would have confused the determination of the effect of nasopharyngeal irradiation on this form of hearing impairment to have included in the calculations the opposite ears, some of which had good hearing and some of which had impaired hearing for all tones. Comparison of Figs. 1 and 3 shows that the baselines, *i.e.*, the averages of their first audiograms, differ for the high tones in the untreated and the treated groups in the manner that would be expected from the basis used for the selection of children for treatment, but that the average *changes* in the acuity of hearing that occurred in the two groups during the period of observation resemble each other closely. The treated group, like the untreated, had a slight improvement in thresholds for tones of the low range of frequencies and a slight

additional impairment for high tones. The only real difference in the *changes* that occurred in the average acuity of hearing of the two groups is that the improvement at the low frequency end of the scale includes, in the treated group, the tones of the frequencies of 512 and of 1024 cycles, as well as the ones from 256 downwards. The average changes for the high tones are all slight in amount in the treated group, and the only one for which the average threshold improved at all, from 2048 cycles upwards, was 10321. The average gain at this frequency amounted to only one decibel.

It is well recognized that a hearing impairment limited to high tones may be of the so-called "gradual" type or of the so-called "abrupt" type. The differentiation, which is not always clearcut, is usually made nowadays on the basis of the appearance of the threshold audiogram.[10] To determine whether the effect of nasopharyngeal irradiation may differ with the type of high-tone loss, the material used for Fig. 3 has been subdivided.

The "gradual" high-tone losses. Fig. 4, A, presents the data for the 43 ears that had, individually considered, an impair-

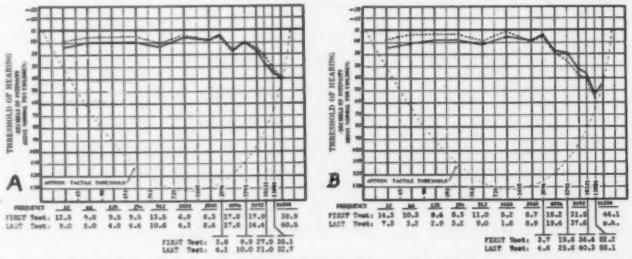


Fig. 4. The high-tone loss cases (see Fig. 3) subdivided on the basis of "gradual" or of "abrupt" type loss at the first test.

ment of the "gradual" type. Even a casual inspection of the charted data shows that in this subgroup a slight gain in average hearing acuity did occur for three of the high tones, those with the frequencies of 8192, 10321 and 13004 cycles per second. A closer scrutiny of the individual records of this subgroup, made in an attempt to learn to what factor the

improvement might be attributed, revealed that only 12 of the 43 ears had an average change, for the four highest frequencies tested (8192 upwards), of more than 10 decibels; nine had become better, three had become worse. Seven of the nine that definitely improved had had a return to normal or essentially normal thresholds for all of the high tones except 16384. It is of interest to note, also, that the three ears for which hearing acuity definitely became worse all had a change in type of high-tone loss, from a "gradual" to an "abrupt" form of impairment; none of the three had undergone a progression of the "gradual" type of loss present at the first examination. Nothing has been found, in the form of relationships to other items about the condition of these children, to explain why some ears of this subgroup had definite changes in hearing acuity while the majority did not.

The "abrupt" high-tone losses. Fig. 4, B, presents the data for the 52 ears that had, at the first examination, some form or other of an "abrupt" type of hearing loss for high tones. Inspection of the charted averages of thresholds shows that in this subgroup, as in that of the ears with a "gradual" type of high-tone loss, the improvement for tones at the lower end of the scale includes the frequencies of 512 and of 1024 cycles, but that, in contrast to the other subgroup, hearing acuity for all the high tones has on the average become worse. In order to ascertain whether the progressive impairment for high tones, for the subgroup as a whole, was associated more with one subtype of "abrupt" loss than with another, the material on which Fig. 4, B, is based has been further subdivided on the basis of how many of the high tones were poorly heard at the first examination.[10] This subdivision of necessity makes the number of ears in each category smaller than is desirable for significance. For whatever they may be worth in indicating trends, however, the averages for the categories that contain 6 or more ears each are presented in Fig. 5, parts A to D. Fig. 5, A, shows the averages of the first and of the last audigrams of 20 ears, each of which had, at the first examination, good hearing for tones up to and including the frequency of 10321 cycles, and markedly im-

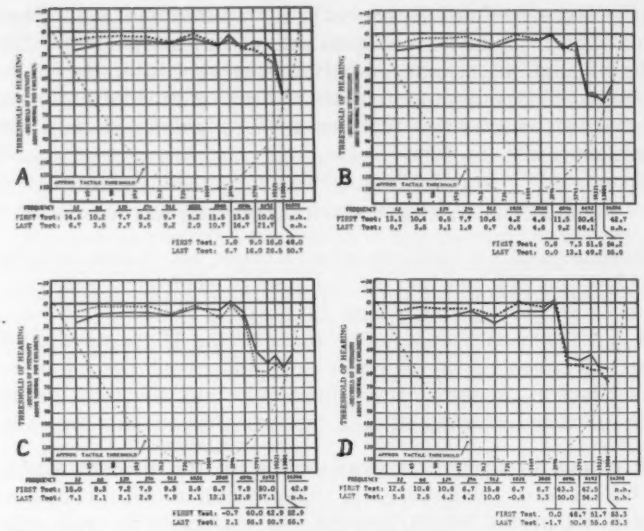


Fig. 5. Subdivision of the "abrupt" type loss cases (see Fig. 4B) on the basis of how many of the high tones were poorly heard at the time of the first test. See text matter for size of groups, etc.

paired hearing, or a total loss, for the two highest tones tested, 13004 and 16384; Fig. 5, B, gives the corresponding data for the 13 ears that originally had the frequency of 5793 cycles as the highest one well heard; Fig. 5, C, gives the data for the 7 ears that at the first examination had markedly impaired hearing for the five frequencies tested above that of 4096 cycles; and Fig. 5, D, gives the data for the 6 ears with which 4096 and all higher frequencies were poorly heard at the beginning of the study.

The progression of the impairment of hearing for high tones that took place in the ears with "abrupt" type losses, as indicated by the observations just presented, occurred in spite of the successful shrinkage, by means of nasopharyngeal irradiation, of lymphoid tissue in the regions of the tubal orifices of these ears. Another item of interest today is that in not even one instance in the entire subgroup of 52 ears was the highest tone that was well heard of a higher frequency

at the last examination than at the first examination. These two facts, in spite of the small size of the categories of the subgroup, afford strong support to the view that the cause of "abrupt" type high-tone losses of hearing in children is not related to the presence or absence of lymphoid tissue in the nasopharynx.[8]

MEDERATE IMPAIRMENT OF HEARING FOR ALL TONES.

Seventeen of the children who returned for re-examination in 1946 or 1947 had had, at the time of their first examinations, a moderate impairment of hearing for all tones; *i.e.*, the thresholds for most tones were in the 25 to 40 decibel zone. In seven of the children the impairment for all tones was bilateral, in ten it was unilateral; thus the total group with impaired hearing of this type consists of only 24 ears.

Previous to their first examination in the present study, all but three of the children in this group had had a suppurative otitis media, which history was confirmed in each case by the appearance of the tympanic membrane, and 12 of the 17 children had had a tonsillectomy and adenoidectomy performed. All of the children were treated by nasopharyngeal irradiation, using radon in a brass applicator with a wall thickness of 1 mm. The usual dosage given at a treatment with this applicator was the equivalent of 2.2 gram minutes of radium, to each side of the nasopharynx. The average number of treatments given the children of this group was $4\frac{1}{2}$; two boys received 8 treatments each. The total irradiation received by each side of the nasopharynx of these two boys was, respectively, 18.7 gram-minutes equivalent in 15 months, and 19.3 gram-minutes equivalent in 21 months. In addition to the irradiation treatments, several of the children had local treatments of the ears, at the times of suppurative episodes, and 4 of the 5 children who had not had a tonsillectomy and adenoidectomy previously had this operation performed during the period of observation. Operation was strongly advised for the fifth child also, but permission for operation was refused by the parents. In other words, treatment of the children of this group was not limited to naso-

pharyngeal irradiation, but efforts were made to improve the hearing by whatever treatment procedure seemed advisable.

On their return in 1946 or 1947, all but one of the 17 children in this small group had normal appearing tubal orifices; this good result includes the boy for whom operative permission was refused. He did have a total of six irradiation treatments during a one-year period of time. Three of the children had, at the time of their return, a suppurating ear.

The average of the audiograms of the 24 ears in this group, at the times of the first and of the last examinations, are presented in Fig. 6. Inspection of the charted data shows

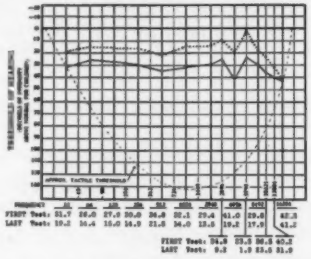


Fig. 6. The averages of the thresholds at the first and at the last tests of the group of 24 ears that had, when first examined (solid line) moderate impairments of hearing for all tones. All had nasopharyngeal irradiation, some had other treatment also. See text matter.

that on the average these ears had a real improvement in hearing acuity during the period covered by the study. Inspection of the individual records shows that none of the ears became markedly worse, that several of them had only slight improvements, and that about half of the ears had marked degrees of improvement. In Fig. 7 are presented the first and

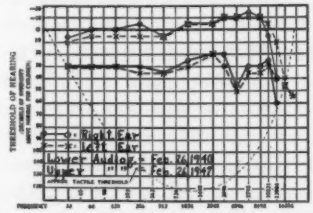


Fig. 7. The actual audiograms (not averages, as in the other figures of this paper) of the child whose hearing improved the most of any during the period of the study

last audiograms of both ears of the child who had the most improvement of any; the interval, it will be noted, was 7 years. Most of the improvement occurred soon after the first two irradiation treatments were given; he had a total of five treatments and received no other throat or nose therapy between the times of the tests charted. He did not have any remissions of hearing acuity during the 7 years. It is of interest to note that this boy, also the two others who had a similar amount of bilateral improvement of hearing, still complained of having frequent colds. The present report is not concerned with evaluation of the effect of nasopharyngeal irradiation on throat and nose infections, therefore this aspect of the more general topic of the Symposium will not be pursued further today.

SEVERE IMPAIRMENTS OF HEARING.

To cover the topic indicated by the title of this report, data with respect to the effects of nasopharyngeal irradiation on the hearing of children who have severe types of impairment should be included. Such data are not available, at least not data based on significantly large groups of children who have been re-examined after time intervals comparable to those for the groups that have been reported today. As was stated early in the report, the method of selection used in 1939-1940 automatically excluded from the study children with hearing impairments so severe that they were not attending regular school classes. Considerable numbers of children with various forms of severe hearing impairment have been treated by irradiation as private patients of my associates, but only small numbers of them, within any one category of types of hearing impairment, have been followed and re-examined five years or longer after the first hearing tests. The question of the possible significance of the data about these small groups (the largest contains only five children) is further complicated by the factors that determine whether private patients continue to return for observation; certainly such groups do not represent a random selection of the patients seen but tend to be biased in favor of those who were not satisfied with the results obtained. Perhaps that is why the data, such as they

are, for the severe types of hearing impairment, show that none of the groups had an average improvement in hearing thresholds. Individual cases, yes; groups, no.

DISCUSSION AND CONCLUSIONS.

The data yielded by this follow-up study of school children indicate that previous ideas of the effect of nasopharyngeal lymphoid tissue on hearing and of the effect of nasopharyngeal irradiation on impaired hearing need to be revised.

The reports and statements that have previously been made on this subject, and the impressions they have given, are well known to most members of this audience, therefore I will not take time in this Symposium to review or to discuss them.[4,5,6,7,13] It suffices for the present to point out that the data from the follow-up study reported today do not support the idea that the most common form of impaired hearing found in children, namely, an impairment of thresholds limited to high tones, is usually a result of interference with the normal functioning of the Eustachian tube due directly or indirectly to the presence of lymphoid tissue in the nasopharynx. Nor do the data reported today support the idea that shrinkage of the nasopharyngeal lymphoid tissue by irradiation favorably affects the thresholds for high tones in many children whose impairments are limited to the high tones of the audible range.

The changes that did occur in the hearing of the children who had impairments only for high tones and who were treated by nasopharyngeal irradiation are, in fact, on the average similar in magnitude and in kind to the average changes that occurred during the same period of years in the hearing thresholds of the large group of children who had good hearing for high tones and who were not treated. If ageing was responsible for the changes in hearing acuity in the latter group (see discussion below), the same factor, ageing, suffices to explain the changes that occurred in the treated group. Whatever the cause of the changes, certainly the similarity of the average changes in the hearing thresh-

olds in the two groups of children warrants the conclusion that the nasopharyngeal irradiation treatments received by the children with impaired hearing for high tones had no effect on their acuity of hearing, either beneficial or otherwise. The question of why the baselines of the two groups, for high tones, were different at the beginning of the period of observation falls outside the province of this Symposium.

For the small group of children who originally had impairments of thresholds for all tones, the audiograms of the first and of the last examinations show that on the average a considerable improvement in hearing acuity occurred during the period of observation. Whether or not the improvement was a result of the treatments received is open to question. Inspection of the individual records of the children in this group reveals a lack of homogeneity of important factors that is in marked contrast to the similarity of the individual records of the children of the groups with various forms of impaired hearing for high tones only. Furthermore, most of the average improvement shown in the audiogram is attributable to the inclusion in this group of three children whose hearing, bilaterally, returned to essentially normal. Such improvements in hearing are well known to occur spontaneously sometimes in children who have moderate impairments of hearing for all tones. A suitable control group of untreated children, followed for a similar period of years, is not available for evaluation of the factor of spontaneous improvement of hearing. For the above reasons I believe that the follow-up study reported today does not contain enough evidence to be convincing with respect to the effect of nasopharyngeal irradiation on the hearing acuity of children who have impairments of thresholds for all tones.

In connection with the above discussed group, it is of interest to note that only 38 of the 1365 children examined in the original survey during the school year 1939-1940 had impaired hearing for all tones, either with one or with both ears, and that 30 of these 38 children either had previously had, or had at the time of the first examination, a suppurative otitis media.[12] The well recognized importance of suppurative otitis

media as a cause of handicapping degrees of impaired hearing is confirmed by the observations, but the data of the present study afford no evidence as to whether or not the incidence of ear infections in early childhood is actually reduced by nasopharyngeal irradiation.

The changes that occurred in the hearing thresholds of the group of 259 untreated children are in some respects the most interesting of the findings made in this follow-up study. All of the children of this group had at least fairly good hearing at the time of their first examinations and none of them had any treatment of ears, nose or throat during the period of observation. The changes that occurred may therefore properly be regarded as normal for the age period covered. The fact that, for the group as a whole, a slight loss occurred in the thresholds for very high tones, is in good agreement with what was to be expected from all the studies that have been made of normal age changes in adults.[1,2,3,11,14,15] The studies of adults, however, have given no reason to expect that an improvement in hearing acuity for low tones occurs during the childhood years. This observation therefore requires further consideration. Three items favor the view that the recorded changes in thresholds actually represent a gain in hearing acuity for low tones. The items are: (1) the care that was taken throughout the study to maintain uniform, and proper, conditions for the making of hearing tests; (2) the fact that all the subgroupings that have been made of the material, including ones that have not been presented today, show similar changes in the average thresholds for the low tones (32, 64, 128 and 256 cycles) during the period of observation; and (3) the likelihood that any so-called "practice effect" would have been operative for the responses to all of the tones used in the tests, not limited to the responses made to tones of one range only.

I believe, but have no evidence to support the hypothesis, that the above recorded "normal" improvement in thresholds for low tones is the result of a purely physical phenomenon, most probably a change in acoustic impedance related in some way to growth changes in the average size of the middle ear

cavity and the external auditory canal. I doubt that the improvement in hearing which appears to occur normally during childhood, for low tones, results from any organic changes in the inner ear or in the auditory pathways of the brain. Certainly the observations reported today rule out spontaneous regression of lymphoid tissue in the region of the nasopharyngeal orifice of the Eustachian tube as the remote cause of the improvement under discussion, which occurred also in the group of children in whom spontaneous regression did not occur and in the group that had normal appearing tubal orifices throughout the period of observation.

The average change in hearing acuity for low tones that occurred in the children is so small that it would not be considered significant in comparing tests of an individual, but it occurred so consistently in the groupings of the material of the present study that I believe it to be a fundamental phenomenon in the age changes related to hearing; certainly it should be looked for by others who have material suitable for the purpose.

SUMMARY.

The title of today's Symposium stresses the irradiation aspect of the basic topic, which is lymphoid tissue in the nasopharynx. The data of the follow-up study of school children reported above yield information about the broad aspect of the relation of nasopharyngeal lymphoid tissue to hearing acuity as well as information about the effect on hearing thresholds of treatment of this tissue by irradiation.

The shortest interval between the first and the last hearing tests of the children in this study was six years, the average interval was slightly over 6½ years, both for the treated and for the untreated children. The average age of the children at the time of the first examination was 9½ years; the age range at that time was from 8 to 13 years.

In a group of 259 children (518 ears) whose hearing was good at the first examination and who had no throat treatment, either irradiative or operative, during the entire period

of the study, a slight average gain in hearing acuity occurred for low tones, as measured by audiometric air-conduction thresholds, and on the average a slight loss occurred for high tones. The gain for low tones occurred consistently in each of the subgroups based on the four possible combinations of normal or of abnormal tubal orifices at the beginning and at the end, respectively, of the period of observation. One subgroup, however, had on the average no loss for high tones; it consists of 53 children (106 ears) whose tubal orifices were abnormal in appearance, on nasopharyngoscopic inspection, at both the first and the last examinations. The greatest average loss for high tones occurred in the subgroup of 63 children who had normal appearing tubal orifices at the beginning and at the end of the study.

A group of 95 ears of children who had impaired hearing only for high tones, either bilaterally or unilaterally, and who were treated by irradiation of the nasopharyngeal lymphoid tissue, showed an average gain for low tones similar to that in the untreated children, in whom it is regarded as normal for the age period, and a slight additional loss for high tones. In no instance of the 52 ears that had an "abrupt" type of high-tone loss was the highest tone that was well heard of a higher frequency at the last examination than it was at the first examination.

A group of 24 ears that had a moderate impairment of hearing for all tones — "flat" audiograms at the 25 to 40 db. level — had, as a group average, real improvements in hearing acuity for all tones, after irradiation of the nasopharynx. About half of them, however, showed either very little or no improvement in hearing acuity.

The broad conclusion is reached that previous ideas, widely prevalent, of the effect of nasopharyngeal lymphoid tissue on hearing and of the effect of nasopharyngeal irradiation on impaired hearing, need to be revised.

REFERENCES.

1. Bunch, C. C.: Age Variations in Auditory Acuity. *Arch. Otolaryngol.*, 9:625-636, June, 1929.

2. BUNCH, C. C., and RAIFORD, T. S.: Race and Sex Variations in Auditory Acuity. *Arch. Otolaryngol.*, 13:423-434, Mar., 1931.

3. CIOCCO, A.: Observations on Hearing of 1980 Individuals. A Biometric Study. THE LARYNGOSCOPE, 42:837-856, Nov., 1932.

4. CROWE, S. J.: Irradiation Treatment of Hyperplastic Lymphoid Tissue in the Nasopharynx, *Chapter in* Diseases of the Nose, Throat and Ear, edited by Chevalier Jackson and C. L. Jackson. Philadelphia: W. B. Saunders Co., 1945.

5. CROWE, S. J.: Irradiation of the Nasopharynx. *Trans. Am. Acad. of Ophthalmol. and Otolaryngol.*, pp. 29-35, Sept.-Oct., 1946.

6. CROWE, S. J.: Infections of the Nasopharynx, Their Causes and Treatment. *Trans. Am. Otol. Soc., Inc.*, 36:17-40, 1948.

7. CROWE, S. J., and BAYLOR, J. W.: The Prevention of Deafness. *Jour. A. M. A.*, 112:585-590, Feb. 18, 1939.

8. CROWE, S. J.; GUILD, S. R., and POLVOGT, L. M.: Observations on the Pathology of High-Tone Deafness. *Bull. Johns Hopkins Hosp.*, 54:315-379, May, 1934.

9. CROWE, S. J.; GUILD, S. R.; LANGER, E.; LOCH, W. E., and ROBBINS, M. H.: Impaired Hearing in School Children. THE LARYNGOSCOPE, 52:790-804, Oct., 1942.

10. GUILD, S. R.: A Method of Classifying Audiograms. THE LARYNGOSCOPE, 42:821-836, Nov., 1932.

11. GUILD, S. R.: *Chapter on* The Ear, in Problems of Ageing, Medical and Biological Aspects, edited by E. V. Cowdry. Baltimore: Williams and Wilkins Co., 2nd Ed., 1942.

12. GUILD, S. R.; POLVOGT, L. M.; SANDSTEAD, H. R.; LOCH, W. E.; LANGER, E.; ROBBINS, M. H., and PARR, W. A.: Impaired Hearing in School Children. THE LARYNGOSCOPE, 50:731-746, Aug., 1940.

13. PROCTOR, D. F.; POLVOGT, L. M., and CROWE, S. J.: Irradiation of Lymphoid Tissue in Diseases of the Upper Respiratory Tract. *Bull. Johns Hopkins Hosp.*, 83:383-424, Nov., 1948.

14. ZWAARDEMAKER, H.: Der Verlust an hohen Tönen mit zunehmenden Alter: ein neues Gesetz. *Arch. f. Ohrenh.*, 32:53-56, 1891.

15. ZWAARDEMAKER, H.: Das Presbyacusische Gesetz. *Ztschr. f. Ohrenh.*, 24:280-287, 1893.

OBSERVATIONS THROUGH COCHLEAR FENESTRA.*†

H. B. PERLMAN, M.D.,
Chicago, Ill.

The development of our concepts of the physical phenomena taking place in the cochlea during acoustic stimulation has been largely dependent upon the study of the anatomy of the cochlea, particularly as observed in microscopic sections. The bioelectric and psychological phenomena have also been used as a base for our interpretations of the mechanics of cochlear function. In spite of a tremendous amount of thought and effort dating back to De Verney, in 1683, the separation of the purely physical from the neural phenomena in the cochlea remains obscure. The solution of this problem is necessary for an orderly development of our understanding of the function of this small complicated peripheral acoustic receptor.

Great difficulty in direct inspection of the cochlea during acoustic stimulation has also led to the use of models for clarifying the physical processes that may occur within the cochlea in response to acoustic stimuli. Models have been constructed on conceived rather than measured physical properties of the cochlea. Gradually, as the result of all these varied observations, some form of frequency selectivity in the cochlea has been agreed upon by most observers.

Direct observations of the cochlea during acoustic stimulation have been strikingly absent from the extensive background of anatomical and physiological studies upon which our concepts of cochlear function are based. We are indebted to Békésy[1,2] for working out the methodology for making direct observations on the cochlea during static and acoustic

*This work was done in part under a grant from the Douglas Smith Foundation for Medical Research of the University of Chicago.

†From the Division of Otolaryngology of the University of Chicago.

Editor's Note: This ms. received in Laryngoscope Office and accepted for publication, Nov. 12, 1949.

pressure stimulation and for contributing most of the known facts about the physical properties of the cochlea and its reaction to acoustic stimulation. Békésy, using new techniques, during the past decade has presented a great deal of new fundamental information about the physical responses of the cochlea. He first made direct observations on the volume elasticity of the basilar membrane and the cochlear duct and found that the elastic component of the mechanical impedance of the basilar membrane varied from apex to base by a factor of about 100 to one.

The above statement, using the term mechanical impedance, needs some clarification for the clinician.

Any structure will offer mechanical impedance to vibration. Such impedance is due to three fundamental properties: mass, elasticity and friction. When a driving force acts to set a structure into vibration, forces which tend to resist the motion result from these three fundamental properties which are, respectively:

1. An inertia force due to the mass.
2. A stiffness due to elasticity.
3. A resistance force due to friction.

The effects of these three properties are combined mathematically into a single quantity, known as the mechanical impedance of the structure to vibration. The amplitude of vibration is directly proportional to the amplitude of the driving force but inversely proportional to the mechanical impedance.

At every point along the cochlea, the structures of the cochlear duct offer a form of mechanical impedance to the driving forces in the perilymph. All but one of the structures of the cochlear duct yet studied exhibit relatively constant impedance throughout the entire length. The basilar membrane, however, has been found by Békésy to have a varying impedance along its length, its impedance being highest at the base and lowest at the apex. That is, the amplitude of displace-

ment of the basilar membrane under static pressure varies by a factor of 100 to one from apex to base. This is a measure of the elastic component of impedance.

Békésy observed that the shape of the depression of the basilar membrane to a point source does not indicate that the membrane is under any special transverse tension, but suggests rather that the membrane responds as an unstressed gelatinous plate with varying volume elasticity. Using an artificial stapes so as to maintain a constant amplitude or volume displacement of the stimulus, he studied through suitable windows the nature of the vibrations induced and found that there was a region of maximum amplitude of vibration of the cochlear duct. This region changed with the frequency of the stimulus. He found,[3] probably for the first time, a definite frequency distribution along the basilar membrane for frequencies between 25 and 2000 cycles per second. He then determined the pattern of response at a given position on the membrane for varying frequencies with constant amplitude and volume displacement of the stapes. This indicated that from a given point along the basilar membrane there was a rather wide flat frequency response instead of a sharply peaked response to a very narrow frequency band. The frequency response was that of a considerably damped vibration. The high damping was corroborated by other ingenious methods of observation, *i.e.*, using a rotating objective in the microscope, and was measured.[4]

The apical end of the cochlear duct was seen to vibrate maximally to very low frequencies and to stop vibrating as the frequency of stimulation was raised. Békésy[5] has already measured the volume displacement of the round window for sounds of constant pressure at the drum and found that the volume displacement of the round window was rather uniform for frequencies up to about 3000 cycles. For a large sound pressure this volume displacement was about one-millionth of a cubic centimeter. The amplitude of the movement of the cochlear partition for this stimulus was about one-thousandth of a millimeter. For acoustic stimuli of constant amplitude the basilar membrane, therefore, moved less for low frequen-

cies, since a longer segment of the membrane was set into vibration than for high frequencies where the apical end was by-passed and no longer vibrated. For a constant volume displacement of the stapes the amplitude of vibration of the basilar membrane to higher frequencies was increased only by a factor of 10 to one, and while it was in the right direction to explain the increased sensitivity of the ear at high frequencies over the low frequencies, the increase was of much smaller amplitude than that observed in the human auditory threshold. Physical laws indicated that the continuously varying mechanical impedance of the basilar membrane would result in a continuously varying velocity of the wave of deformation as initiated by the moving footplate. He measured,[4] for various positions near the apical end of the cochlea, the velocity of propagation of a sharp pulse. A sharp pulse initiated at the stapes arrived 1/1000 second later 25 mm. away on the basilar membrane. This was the region responding maximally to 500 cycles per second. By a remarkable experiment[6] he found that the movement of the basilar membrane is in phase with that of the stapes only at very low frequencies and as the frequency is increased there is an ever greater phase lag between footplate movement and movement of basilar membrane. This indicated that the stimulus is propagated as a traveling wave, becoming shorter as the frequency is increased; however, all these stimuli travel along the basilar membrane with varying velocity, being rapid at the narrow end and slowing down as they reach the region of maximum response. Beyond this region the disturbance rather rapidly dies out.

The conducting mechanism has long been known to be acoustically active in the fresh cadaver and even when the fresh temporal bone is removed from the cadaver and kept in a cold, moist chamber. Many important physical properties of this mechanism in response to sound have been determined with such preparations. The state of the tissues and fluids within the labyrinth during acoustic stimulation has been more obscure, but with fresh and properly preserved specimens it can easily be shown that many of the structures seen

under the microscope in temporal bone sections can be visualized in action in the fresh state. This has been clearly demonstrated to the clinician in the living human ear where the membranous semicircular canal and ampulla can be identified and manipulated during fenestration and even partially evulsed as in the surgical treatment of Ménière's disease. Similar observations in the fresh human cadaver preparation reveal that these parts of the membranous labyrinth are also easily demonstrable. In these preparations the fluid in the labyrinth is preserved and the membranous canal can be stretched and partly evulsed as in the living ear. It can be freed from its attachment to the bony canal, compressed and moved about and perforated. Some conception of the physical character of the endolymph can be obtained.

The modern methods of exposure of the labyrinth spaces under a dissecting microscope, using dental drills of various degrees of size and fineness with irrigation of the area to remove bone dust, has been highly developed by Békésy and permits the creation of clean fistulas in these specimens opening into almost any part of the labyrinth, including the various coils of the cochlea. The use of normal saline or Ringer's

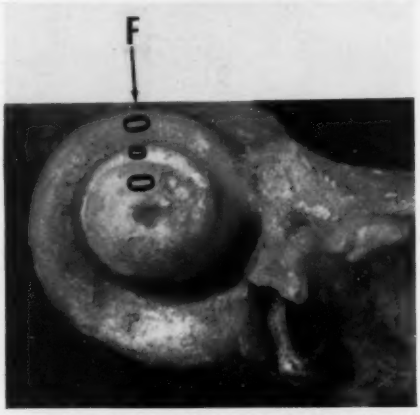


Fig. 1. Dissection of the bony cochlear capsule indicating the approximate size and location of the fenestra (F) that can be made looking into the scala vestibuli of the apical, middle and basal coil while still preserving the conducting machinism for transmission of the acoustic stimulus.

solution for irrigation is useful to prevent trauma to the membranous wall of the cochlear duct due to osmotic tension differences. Using a binocular microscope, usually with a 30 to 70x magnification, or a water immersion lens for magnification up to 150x, the structures within the cochlea are made available for study.

The petrous pyramid is cleaned and the tensor tympani muscle is partially removed with its bony partition so that the area of the apex and middle coil of the cochlea can be exposed while still preserving the conducting mechanism. Some of the basal coil can also be exposed in this way from the scala vestibuli side (see Figs. 1, 2, 3). As Békésy has

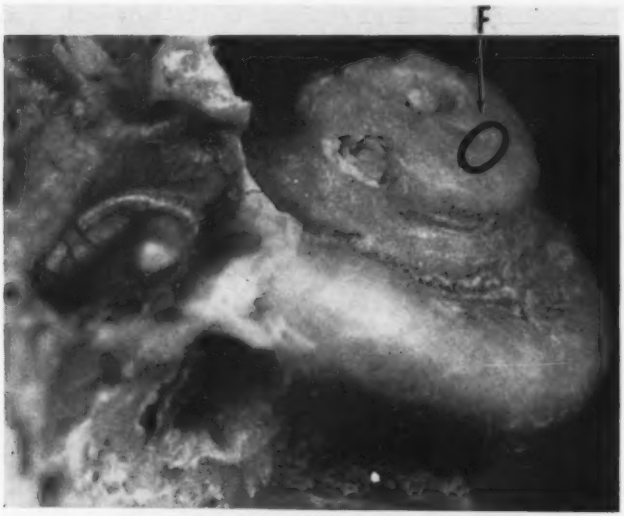


Fig. 2. Cochlear capsule as viewed from the labyrinth windows. Oval area indicates approximate size of observations window (F) used in these experiments.

shown, exposure of the basal coil nearer to the vestibule can be obtained by drilling out the internal acoustic meatus and opening the scala tympani of the basal coil for a view of the

Fig. 3. View of round window area (RW) of the cochlea in a human fetus at birth with the beginning of the basal coil in focus. Oval area indicates the approximate size of observation windows (F) used. The head of the stapes is indicated by (S).

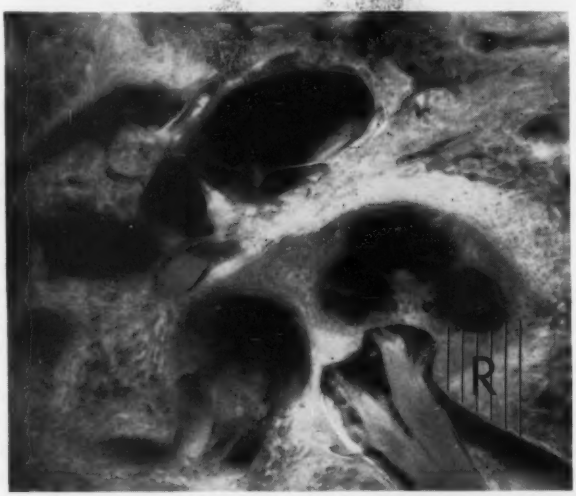


Fig. 4. Cross-section of the cochlea indicating the relative position of the bone removed (R) at the internal meatus for the creation of an observation window looking into the scala tympani of the basal coil close to the vestibule. The spiral ligament, basilar membrane and spiral lamina of the basal coil are clearly seen.

basilar membrane and spiral lamina (see Figs. 4, 5). In this manner the cochlear structures can be visualized and the fluid within the cochlea can be preserved. Through these windows it is easy to recognize the Reissner's membrane, spiral ligament and spiral lamina. Reissner's membrane and other membranous structures can be more clearly delimited and observed during acoustic movement by placing specially prepared highly

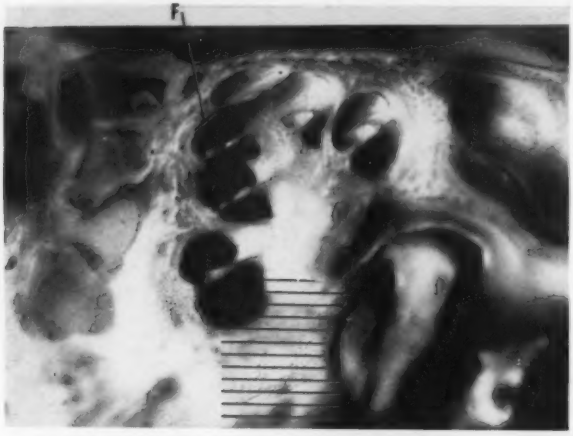


Fig. 5. Cross-section of the cochlea to indicate the position of the observation windows (F) relative to the cochlear duct. Reissner's membrane is clearly seen. Shaded area represents capsule bone removed at the internal meatus to expose the proximal end of the basilar membrane.

reflecting silver crystals in the perilymph and allowing them to settle and adhere to the membranous and bony structures.

The instruments needed to manipulate these cochlear structures in the fenestra consist of various sized hairs fixed to the end of a wooden applicator or glass rod. Fine glass, platinum or palladium probes can also be made in this way. Steel needles, straight and shaped into fine hooks, are used as in a fenestration operation to remove bone fragments from the edge of the fistula to open the endosteum and remove fragments lying on the cochlear duct, etc.

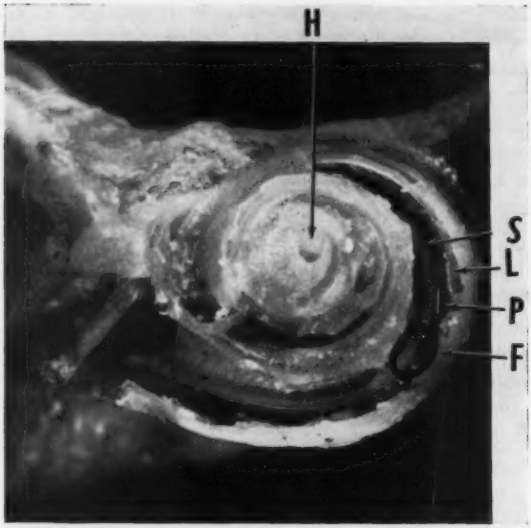


Fig. 6. Widely opened cochlea to show the relation of the scalae, the bony spiral lamina and basilar membrane. Oval area indicates approximate size of field exposed by fenestra (F). A white line (P) is placed on the basilar membrane above fenestra to indicate relative thickness of hair probe used through the fenestra to depress the basilar membrane and manipulate Reissner's and the tectorial membrane. An arrow points to the spiral ligament (L) detached from the cochlear capsule and another arrow points to the edge of the bony spiral lamina (S) to which the basilar membrane is attached. The helicotrema can be made out at (H).

It is easy to tear Reissner's membrane and thus to obtain a direct view of the basilar membrane and its superimposed structures. While the details of the organ of Corti cannot be made out, the tectorial membrane is easily visualized as a flat ribbon of gelatinous material near the free lip of the bony spiral lamina and appears to be adherent to the cells on the basilar membrane below it (see Fig. 5).

The tectorial membrane can be lifted off these cells and a long ribbon of tectorial membrane can be freed. This tectorial membrane has considerable resistance to tearing, coming away from a large area. It can even be delivered out of the observation window before the fine hook or needle succeeds in breaking it as it is lifted off the basilar membrane. As Békésy[6] has observed, point pressure on the tectorial membrane pro-

duces an elongated hollow depression in contrast to the other surfaces that exhibit a circular depression. The tectorial membrane exhibits a different elasticity in the transverse direction than it does lengthwise. In the lengthwise direction it is more stiff. According to Békésy, the reduced stiffness in the transverse direction, peculiar to the tectorial membrane, permits a pressure drop along the cochlear duct that favors frequency analysis.

The basilar membrane can be depressed with a fine human hair or fine metal rod, and a judgment of its volume displacement or the elastic component of its mechanical impedance at various positions along the cochlea can be determined. The limits of its width are easily seen as it bridges across as an almost transparent sheet from the spiral bony lamina to the spiral ligament (see Fig. 6). The shape of the deformation of the basilar membrane to a point pressure indicates that it has no special transverse tension as compared to its longitudinal tension. The depression is shallow and circular through most of its length. The basilar membrane may also be perforated with either a human hair or a fine wire. The shape of the hole so produced through most of the basilar membrane is circular and again indicates that it is exposed to equal forces in the transverse and longitudinal direction. On the basis of this response to pressure by a point source, Békésy likens the basilar membrane to an unstressed gelatinous plate. Using hairs of graduated and measured stiffness and by using a constant pressure of 1 cm. water, Békésy has obtained quantitative judgment of the elasticity or stiffness of the basilar membrane. The membrane is exposed to restoring forces since it returns from its displaced position when depressed with a probe. Békésy showed that movement of the cochlear partition imparted by acoustic stimuli dies out rapidly, indicating considerable damping. The degree of stiffness of the basilar membrane is easily seen to vary along the cochlear duct when observing the amount of deformation to a probe of suitable stiffness. The membrane is more stiff in its narrow basilar portion and relatively more movable at its apical or wide end, where, indeed, the modiolus and bony lamina

can also be moved but with greater forces. At this end the helicotrema can be clearly visualized with its terminal portion of the cochlear duct (see Fig. 7). This area is rather difficult

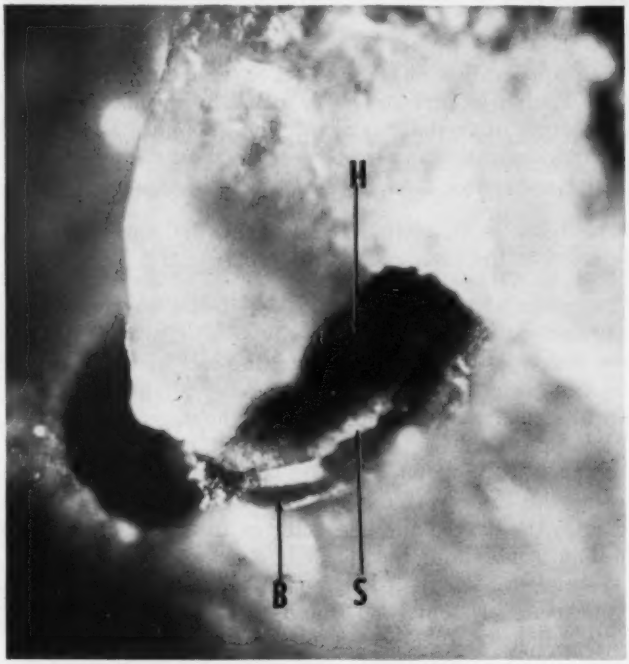


Fig. 7. Dissection indicating the portion of the helicotrema (H) relative to the end of the bony spiral lamina (S). The basilar membrane is indicated at (B). The thickness of the arrow corresponds to that of the fine probes used to depress the basilar membrane or manipulate Reissner's and the tectorial membrane (not shown in the illustration).

to expose without tearing the Reissner's membrane or fracturing the modiolus. Békésy found a variation from the wide apical end to the narrow basal end of 100 to one in volume displacement of the basilar membrane to a constant static pressure of 1 cm. water.

The spiral ligament can be observed as it is moved by a hair probe and it can be easily peeled from its attachment to the outer bony cochlear wall (see Fig. 6). The ease with which

this structure can be peeled from the outer wall and the retention of its form and that of the basilar membrane, even when so freed by the cochlear fluids, indicate that no real ligamentous pull on the basilar membrane is carried out by the spiral ligament.

The appearance and the marked resistance of the bony spiral lamina to pressure with a fine hair easily defines the medial limit of the basilar membrane. The medial edge of the basilar membrane can also be seen as the location of the tectorial membrane.

The bony lamina with the rest of the modiolus can be inspected in the area exposed by the fenestra.

The greatly reduced resistance of Reissner's membrane to deformation with a probe is easily seen, also its rather uniform degree of resistance all along the cochlear duct. The flat 0.04 mm. wide silver crystals are excellent light reflectors and help to visualize more quantitatively the degree of movement of Reissner's membrane when touched by a hair probe or when moved by sound stimuli. There and elsewhere in the cochlea the change of the point of light into a line or oval indicates the degree and character of the resultant vibration. The fluid contents of the cochlear duct are qualitatively seen to resemble that of the perilymph. This is in marked contrast to the tectorial membrane that is seen as a thin gelatinous ribbon adhering to the cells on the basilar membrane.

The response of these various identifiable and visible structures of the cochlea to acoustic stimuli reaching it through the intact conducting mechanism can be observed by so preparing and imbedding the specimen that the conducting mechanism is preserved along with the external canal and only the cochlear area is exposed for fenestration.

Strong light reflected by a small mirror mounted on the microscope and focused to a fine point is needed to illuminate properly the structures within the 2 mm. fistula, using up to 70x magnification with the stereomicroscope. A water immersion lens with the apex of the petrous pyramid immersed in

saline may be used for higher magnification while protecting the middle ear mechanism from filling with fluid during acoustic stimulation. The illumination of an "ultra pack" can also be used here. For acoustic stimulation the external canal is coupled through tubing to the loud speaker driver unit activated by a Hewitt Packard audio-oscillator and suitable amplifier.

For greater facility in making manipulations and exposing the structures within the fistula, the plaster imbedded bone is mounted in a clamp with a universal joint so that movement in all directions is possible. The area about the binocular scope is surrounded by a platform for a more secure rest of the operator's arms. The scope is mounted directly to the table top. With practice and with the arms placed in the same position and the instruments grasped in about the same position on the handle, they can be brought into the small field, about 3 mm.^{2} to 6 mm.^{2}, rather consistently.

The temporal bones of other mammals (see Fig. 8) (guinea pig, cat, etc.) can be similarly prepared and investigated for static and acoustic characteristics of the cochlea (Békésy[7]). The temporal bone in the human is more difficult to work with because of the relatively great thickness of the cochlear capsule, but when the bones from a newborn are used, this is greatly facilitated. Most of our observations in the human were made on full-term fetal temporal bones with aerated middle ears. Since the conducting mechanism and the cochlea are quite fully developed at birth, satisfactory information can be obtained. The amount of capsule bone that must be removed is minimal in these specimens. Stroboscopic illumination with a strobotac as well as constant illumination may be used for making observations of acoustic responses. Silver crystals, bone dust and lamp black particles suspended in the cochlear fluids can be observed for evidence of the behavior of the fluids in the cochlea during acoustic stimulation.

With the experimental procedure described, the great amount of activity observed in the fluids and membranous structures within the cochlea during acoustic stimulation

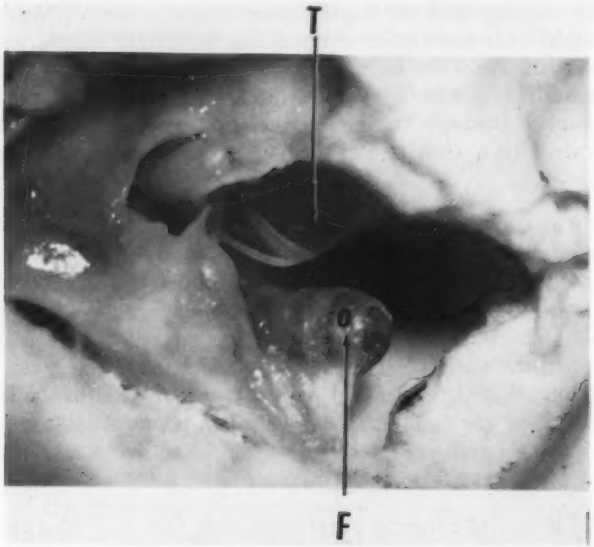


Fig. 8. Exposure of guinea pig ear with oval area indicating approximate size of fenestra (F) used for observing through the binocular scope, with about 60× magnification, the activity within the various coils of the cochlea during acoustic stimulation through the intact ossicular chain. The drum (T), malleus and incus are easily visualized just above the cochlea.

through the intact chain is striking. A knowledge of the behavior of fluids in motion (hydrodynamics) becomes at once of interest to the observer. For a clearer insight into the observed activity in the cochlea, one is led to a consideration of this relatively new and difficult field of physics. Known laws of fluid mechanics enter into the explanation of the visible activity such as eddy currents seen within the cochlea during acoustic stimulation. The particular structure of the organ of Corti itself, such as the pillars and fluid spaces about them, no doubt control the ultimate definition of the fluid movements that affect the end-organ.

It is possible to observe that the acoustic vibration of the cochlear partition in response to acoustic stimuli entering through the intact conducting mechanism is at right angles to the scalae and that Reissner's membrane moves with the

basilar membrane. The cochlear duct appears to vibrate as a unit. At low frequencies (15 cycles per second), movement of the cochlear fluid on each side of the cochlear duct parallel to the scalae can be observed, as reflected by the action of particles suspended in it. As the frequency of the sound is increased, right angled movements of the cochlear partition are observed with greatest amplitude at the apex. As the frequency is further increased, above about 400 cycles, the apex is seen to come to rest and through windows in the middle and lower coil one sees active vibration of Reissner's membrane, etc. In these preparations this acoustic response can be observed in the basal coil up to about 2000 cycles in man and higher in the guinea pig. Transmission of these high frequencies is inefficient through the air in the coupled tubings between the speaker and the external canal. Movement of the fluid system consists in parallel to and fro pulsasations along the length of the cochlear duct for very low frequencies, eddy current parallel to the length of the cochlear duct exposed by the fistula, and eddy currents at right angles to the cochlear duct. These latter are very striking and can be made to shift with frequency and to change their velocity and radius with change of intensity. The velocity of the right angled eddy current is greatest as it moves past the basilar membrane and is least at the top of its rotation near the level of the observation window. These eddies may be small in diameter, being limited to the area immediately adjacent to the basilar or Reissner's membrane. They can be observed beyond the limits of the fenestra by tilting the preparation. The Reissner's membrane appears to move outward as a static displacement into the scala vestibuli while vibrating acoustically. This is true of the tectorial membrane while still attached and when partially loosened from the underlying cells. The static negative component in the response may be due to the asymmetry of the stimulus delivered by the chain to the cochlea. This stimulus is stronger on the negative side of center. The tectorial membrane can be torn off the underlying cells by large acoustic stimuli. Particles entering the cochlear duct through a tear in Reissner's membrane can be seen to execute eddy movement within the cochlear duct and

at right angles to the basilar membrane. Eddy currents may be limited to the fluid near the cochlear duct or with larger stimuli may involve the fluid inward to the modiolus and up to the bony walls of the scala tympani or vestibuli at the observation window. The acoustic stimuli used to produce these movements are well within physiological limits. For stronger acoustic stimuli the lines of light produced by movement in one plane of a crystal attached to the Reissner's tectorial or basilar membrane can be seen to change into an ellipse, indicating that movement is taking place in more than one plane; that is, at right angles to the cochlear partition and parallel to it. The bony spiral lamina can also be made to oscillate in a complex manner with large stimuli while eddy currents in the fluid over the bony spiral lamina and modiolus are observed.

The frequency discrimination of the cochlea as displayed by the pattern of vibration of the membranous portions of the cochlear partition is a very broad one. The whole cochlear duct appears to be set in vibration by low frequencies while shorter and shorter segments are seen to be involved as the frequency of acoustic stimulation is raised. The wide extent of motion set up by low frequency sounds is in the proper direction to explain the broad masking produced by large low frequency sounds as compared to the narrowing of the masking limits with higher frequency of stimulation. Distinct cessation of vibration of the cochlear partition at the apical window is noted, while the middle coil window reveals very active movement at 400 cycles. Békésy found that for a constant volume displacement of the stapes, the cochlear partition moves with a smaller amplitude at low frequencies than at high frequencies. The variation in amplitude is about 10 to one. This is much smaller but in the direction of the movement of the drum necessary to elicit a threshold response. The drum moves over 1000 times as much at low frequencies at the threshold than at higher frequencies; hence, the threshold characteristics of hearing at low frequencies are not explained by the behavior of the cochlear vibration observed.

A proper judgment of the consistency and mechanical resistance of the basilar membrane to deformation as determined by direct observations upon it permits the construction of models to aid in understanding cochlear mechanics. From his studies in models we are further indebted to Békésy[3] for a clarification of some of the physical dimensions that are important in maintaining a frequency analysis along the basilar membrane.

A V-shaped slit between two razor blade edges inserted over a trough 2 sq. mm. in transverse area is considered by Békésy[3] as the most simple type of model of the cochlea (see Fig. 9). The separation of the razor blade edges approxi-

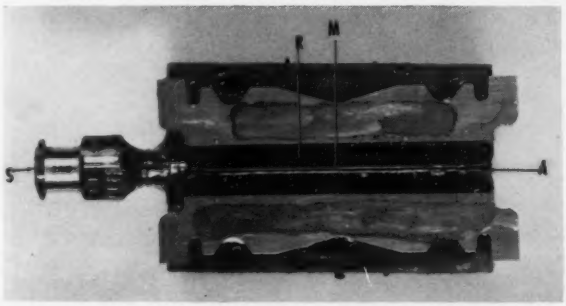


Fig. 9. Photograph of a simplified model of the cochlea, consisting of two razor back edges (R) across which a thin rubber solution is floated to make the basilar membrane (M). The acoustic stimulus is delivered through tubing from a loud speaker driven unit into the needle hub on the left (S). This opens into an air-containing trough (A) under the artificial basilar membrane. Fluid is placed over the membrane and silver, lycopodeum and lamp black particles used to observe the resulting motion.

mates the varying width of the basilar membrane, and the space bridged by floating a thin rubber solution over it. This creates a very thin homogenous elastic plate upon which water is placed with silver crystals, lamp black and lycopodium to observe activity in the superimposed fluid and movement of the artificial basilar membrane. Sound is delivered by air conduction through a sealed-in large gauge hypodermic needle shoulder. Békésy has shown that such a simplified model works in a manner similar to that of a complete model with two fluid-containing chambers separated by the basilar mem-

brane. Responses up to 4500 cycles have been observed in this way with eddy currents at right angles to the membrane and limited to the fluid just above the membrane, instead of involving the entire overlying fluid. Changes in speed of motion in the eddy with respect to the artificial basilar membrane and increased velocity and diameter of the eddy as intensity of the stimulus is raised could be observed as in the cochlea itself as well as shifting of the position of the eddy along the membrane with changing frequency. The present concept of cochlear mechanics based on observations in models and in the cochlea as well as on some physiological experiments is that a wave of deformation of the cochlear partition is initiated by movement of the stapes and is propagated along the basilar membrane to reach a maximum at a position depending upon the frequency. This wave of deformation for all frequencies moves at varying velocity along the basilar membrane, being rapid at the beginning and slowing as it approaches the point of maximum response. The rate of propagation along the basilar membrane varies. For a position 25 mm. away from the narrow end, Békésy measured this velocity and found it to be 40 meters per second. The limits of variation in velocity throughout the entire length of the cochlear duct are now known. This velocity is, of course, much less than that of a sound wave in an infinite fluid medium (about 1500 meters per second and independent of frequency). The varying volume displacement of the basilar membrane along its length determines the rate of propagation and the region of maximum displacement. With higher frequencies the upper end of the cochlear duct is by-passed and the activity is seen to be confined to shorter and shorter segments of the cochlear duct.

The whole cochlear duct appears to vibrate as a unit at right angles to its length while the wave of deformation travels along the length of the duct. The column of fluid in the perilymph between the two windows does not move back and forth as a unit in phase with the motion of the footplate except at very low frequencies, *i.e.*, 15 cycles per second. Below 20 cycles the fluid moves through the helicotrema without affect-

ing the cochlear partition. As the frequency is increased there is right angled movement of the partition and an ever greater phase lag between the movement of the stapes and that of the cochlear partition indicating a wave of motion being propagated along this partition. The distribution of amplitude along the basilar membrane for a given frequency is rather flat and does not provide evidence for a sharp definition of the stimulus; however, Békésy found that the phase of motion at a given position on the basilar membrane with respect to the motion of the stapes can be shifted by a very small change in frequency. Small disturbances in the pattern of vibration with change of frequency are manifested by this shift in phase. According to Békésy, the mechanical volume displacement of the partition together with the mass of the fluid very near to it effect its acoustic response, while the damping is a resultant of these forces and is quite large.

The rôle of the associated eddy current in effecting a pressure stimulation of the end-organ is considered in the mathematical analysis of the cochlea by Ranke[8] but minimized by Zwislocki.[9]

SUMMARY.

Direct measurement of some of the physical properties of the cochlea and observations of the cochlea during acoustic stimulation is possible with modern techniques and offers new important information about the physical processes in cochlear function.

BIBLIOGRAPHY.

1. Bekesy, G. V.: Zur Theorie des Hörens: Die Schwingungsform der Basilar Membrane. *Phys. Ztschr.*, 29:793-810, 1928.

2. Bekesy, G. V.: Uber die Elastizität der Schnecken Trennwand des Ohres. *Akus. Ztschr.*, 6:265-278, 1941. Translation of the above, *Jour. Acous. Soc. Am.*, 20:227-251, 1948.

3. Bekesy, G. V.: Uber die Schwingungen der Schnecken Trennwand Bein Präparat und Ohrenmodel. *Akus. Ztschr.*, 7:173-186, 1942. Translation of the above, *Jour. Acous. Soc. Am.*, 21:233-245, 1949.

4. Bekesy, G. V.: Uber die Resonan und die Abklingzeit der Verscheidenen Stellen der Schnecken Trennwand. *Akus. Ztschr.*, 8:66-76, 1943. Translation of the above, *Jour. Acous. Soc. Am.*, 21:245-254, 1949.

5. Bekesy, G. V.: Uber die Frequenzanalyse in der Menschlischen Schnecke. *Acta Otolaryngol.*, 32:60-84, 1944.

6. BEKESY, G. V.: Variation of Phase Along the Basilar Membrane with Sinusoidal Vibrations. *Jour. Acous. Soc. Am.*, 19:452-460, 1947.

7. BEKESY, G. V.: Uber die Mechanische Frequenzanalyse in der Schnecke Verschiedner Tiere, *Akus. Ztschr.*, 9:3-11, 1944.

8. RANKE, O. F.: Das Massenverhältius Zwischen Membran und Flüssigkeit in Inner Ohr. *Akus. Ztschr.*, 7:1-11, 1942.

9. ZWISLOCKI-MOSCICKI, JOSEF: Theorie der Schencken Mechanik. *Acta Otolaryngol.*, Supp. 72, 1948.

SUGGESTIONS FOR DETERMINING THE MOBILITY OF THE STAPES BY MEANS OF AN ENDOTOSCOPE FOR THE MIDDLE EAR.*†

GEORG V. BÉKÉSY,
Cambridge, Mass.

Hearing losses are usually divided into two distinctly different categories: conductive deafness and nerve deafness. The treatments appropriate to these two defects are different. Although some patients fit neatly into one or the other of these two categories, many cases combine both nerve and conductive defects and are difficult to diagnose. For successful treatment of these combined cases it would be advantageous to know what percentage of the hearing loss is due to each of these two defects. This information might also help answer certain basic questions. For example, can a stapes fixation produce nerve deafness, or are stapes fixation and nerve deafness unrelated processes?

Because of the importance of this and similar questions, some means must be found for making precise diagnoses in combined cases.

DISTINGUISHING BETWEEN NERVE AND CONDUCTIVE DEAFNESS AT AUTOPSY.

It is possible to gain valuable information about the middle ear by making certain physical measurements prior to the histological examination of the cochlea. At autopsy it is possible to measure the conductive loss of a middle ear for the whole frequency range. In the event that it has been possible

*This research was carried out under Contract N5ori-76 between Harvard University and the Office of Naval Research, U. S. Navy (Project Nr147-201, Report PNR-82). Reproduction for any purpose by the U. S. Government is permitted.

†Psycho-Acoustic Laboratory, Harvard University.

Editor's Note: This ms. received in Laryngoscope Office and accepted for publication, Dec. 15, 1949.

to obtain an audiogram before the death of the patient, we can subtract the values for conductive deafness, as measured at autopsy, from the overall deafness and thereby determine the extent of the nerve deafness. Having separated the values for conductive deafness and nerve deafness, we can then correlate them with the histological findings in the middle ear and in the cochlea. This makes the histological findings meaningful in terms of precise functional measurements.

The equipment used to measure conductive loss postmortem is illustrated in Fig. 1. The temporal bone is opened near the

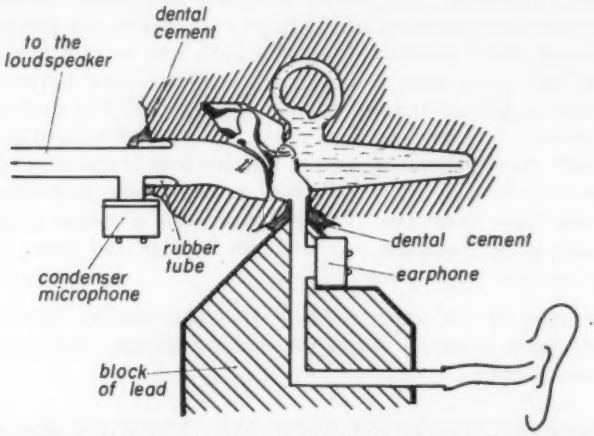


Fig. 1. Equipment for measuring the amplitude of vibration of the round window for a given sound pressure on the eardrum. The sound produced by the movements of the round window is led to the ear of an observer. An earphone is connected to the same tube. If the volume displacement of the round window has the same amplitude, but opposite phase, as the volume displacement of the diaphragm of the earphone, no tone is heard by the observer. In this way it is possible to determine the volume displacement of the round window from the calibration curve of the earphone.

Eustachian tube and a small tube is inserted into the middle ear, just opposite the round window, and cemented into the niche of the round window with an airtight seal. Then the tube and the temporal bone are cemented to a block of lead. A second tube, leading from a loudspeaker is inserted into the ear canal. The sound pressure produced in the ear canal is kept constant by a small condenser microphone. The sound

pressure on the eardrum sets the eardrum into vibration, and with it the stapes footplate and the round window. The vibrations of the round window produce volume displacements of the air in the sealed tube. These air displacements are transmitted through a hole in the lead base to the ear of an observer. The intensity of the sound heard by the observer is a measure of the sound transmitted through the whole ear. For the precise measurement of this intensity an earphone is connected to the observation tube. The phase of the current in this earphone may be so adjusted that the air displacements produced by the earphone are exactly opposite to those produced by the movements of the round window. Then if the magnitudes of these two air displacements are the same, all sound in the tube leading to the ear of the observer is cancelled out and the tone is no longer heard. The amplitude and phase of the current in the earphone, after calibration, give a direct measure of the volume displacement of the round window. The difference between this value and those obtained for normal ears[1] is a measure of the conductive hearing loss in the defective ear.

CORRELATION BETWEEN CONDUCTIVE LOSS AND MOBILITY OF THE STAPES UNDER STATIC PRESSURE.

During an operation it is customary to test the mobility of the stapes by using a fine forceps. The forces acting on the stapes in this case are quite different from those produced by a sound.

For a frequency of 1000 cps with a sound pressure on the eardrum of 10^3 dynes/cm^2, *i.e.*, 1 gm/cm^2, the vibration amplitude of the stapes footplate is only about 2.10^{-5} cm.[2] Since this sound pressure is just below the threshold of feeling, an amplitude of 2.10^{-5} cm is near the maximum that can occur in the audible frequency range without danger of damaging the ear. It is possible that even though the stapes may seem fixated for large movements of the forceps, it may be able to conduct, without any loss, the small vibrations of 2.10^{-5} cm.

In order to measure the mobility of the ossicles at autopsy an opening was made in the roof of the tympanic cavity

without cutting any ligaments. The opening was large enough to expose the head of the hammer and part of the arch of the stapes. A rubber tube was fitted, with an airtight seal, into the ear canal and the temporal bones and ossicles were photographed, first under a positive pressure of 40 mm. Hg., and then under an equal negative pressure. When these two pictures were observed in a stereoscope, the head of the hammer and the arch of the stapes appeared to project from the plane of the temporal bone, provided the ear was normal (see Fig. 2). If the stapes was fixated, however, the arch of the stapes remained in the plane of the temporal bone and only the bulge between the stapes and incus seemed to project forward (see Fig. 3). The distance of the apparent projection from the plane of the temporal bone is a measure of its lateral displacement.

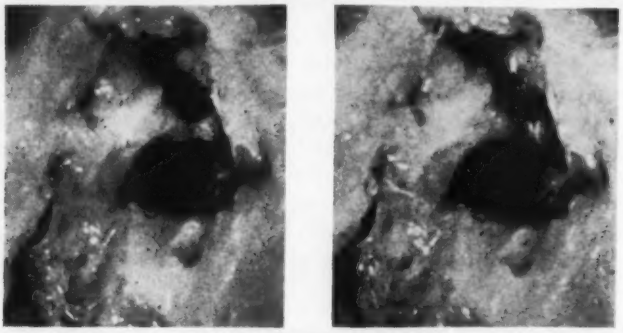


Fig. 2. Stereoscopic photograph of the ossicular chain of the normal ear. Both photographs are of the same temporal bone, first with a pressure of 40 cm. Hg. on the eardrum and then with a suction of 40 cm. Hg. When the pictures are observed in a stereoscope, most of the temporal bone remains stationary and therefore seems to be in a plane. The ossicles are displaced by the changing pressure and they appear, therefore, to jump out from the plane and come closer to the observer.

Since only the horizontal displacements contribute to the three-dimensional stereoscopic effect, for a maximum effect the temporal bone should be turned so that the longitudinal axis of the stapes footplate is vertical and the arch of the stapes, therefore, moves horizontally. Unfortunately shadows produced by the illumination in the photographs of Fig. 2 and Fig. 3 give the surface of the temporal bone a slightly

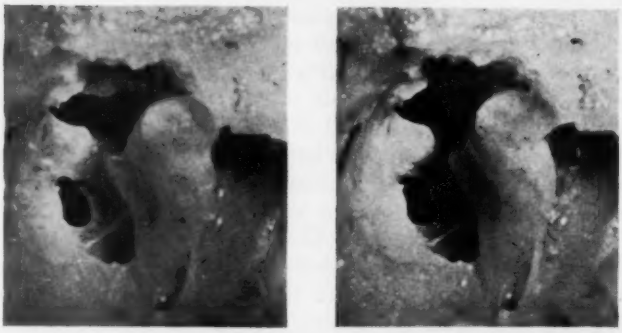


Fig 3. Same as Fig. 2, but for an ear with stapes fixation. The head of the hammer moves about the same degree as in the normal ear, but movement of the stapes is less; therefore, the stapes does not seem to approach the observer to the same extent as in the normal ear.

three-dimensional appearance. In later pictures this effect was overcome by placing a white paper, or mirror, opposite the preparation and taking the picture through a hole in the paper (or mirror).

I had the opportunity to examine four cases of otosclerosis. Comparison of the conductive loss at 1000 cps with the mobility of the stapes, measured by a static pressure, made it clear that a decrease in the mobility of the stapes was always accompanied by a hearing loss for the tone; therefore, it seems possible to predict conductive loss for tones if, under static pressure, there is an observable stapes fixation. When the mobility is tested with forceps, however, no quantitative conclusions can be drawn, because the fixation observed with forceps is apparently the same, whether the hearing loss produced by the stapes fixation is 15 or 40 db.

A POSSIBLE WAY TO DETERMINE THE MOBILITY OF THE STAPES IN A PATIENT.

The stereophotographs with suction and pressure in the ear canal proved so useful with anatomical preparations that we attempted to get X-ray photographs of the ossicles of patients, under positive and negative pressures; but this technique was practically useless because the temporal bones differ so greatly

from individual to individual that it is difficult to get pictures that show the ossicles. One of the reasons for this failure is that the correct positions for such X-ray pictures have not been worked out.

A better method seemed to be to insert a small endotoscope through a perforation in the eardrum, and to observe the stapes directly. A perforation of about 1 to 2 mm. diameter in the eardrum of a healthy person will heal in a few days. During the war it was customary in some countries to perforate the eardrums of fighter pilots so that sudden altitude changes would cause no discomfort. In the case of patients, however, opinion is divided on the matter of the healing of such perforations; but since a perforation in the eardrum does not affect the threshold of hearing in the middle frequency range,[3] this method seems to be justified in cases of combined hearing loss when a correct diagnosis is very important.

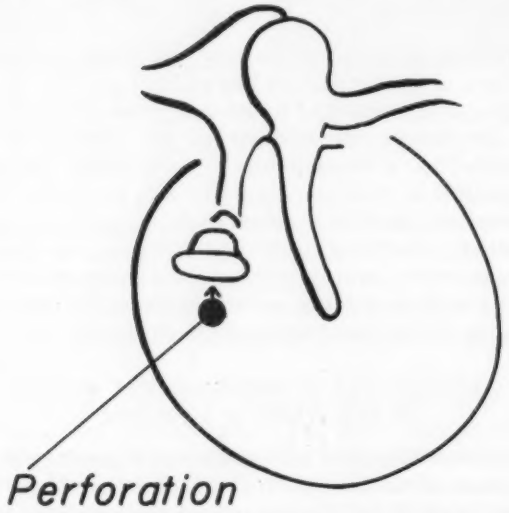


Fig. 4. In order to observe the movement of the stapes in a patient, it is suggested that the eardrum be perforated at the place indicated. The stapes-incus joint can then be observed from below by means of a small endotoscope inserted through the perforation.

A discussion with Dr. Julius Lempert in New York brought out the fact that an endoscope for examination of the middle ear (endotoscope) would probably be of some value. Furthermore, our animal experiments had made it clear that a very small endotoscope would aid in the study of the middle ears of guinea pigs and rats. Consequently we attempted the construction of such an instrument.

Experiments on cadavers showed that the stapes-incus joint can be observed by means of an endotoscope inserted through a hole in the eardrum at the place shown in Fig. 4. The joint is seen from below, as sketched in Fig. 5. On the stapes-incus

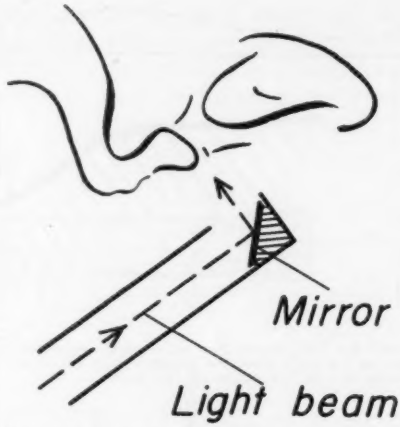


Fig. 5. Path of the light beam in the endotoscope for the observation of the mobility of the stapes.

joint there are two parallel bulges, from which the light is reflected in two sharp streaks. If there is no stapes fixation, pressure acting on the eardrum causes both of these highlights to move, the distance between them remaining the same. The movements are vertical to the longitudinal axis of the stapes footplate. If, however, the stapes is fixated, the distance between the two highlights changes. Thus a stapes fixation can easily be detected.

In order to produce the desired pressure on the eardrum, a test hair of v. Frey was used. The hair was a nylon thread (fish-line leader). It was attached to a small handle, and its other end was blunted with a small ball (see Fig. 6). If this

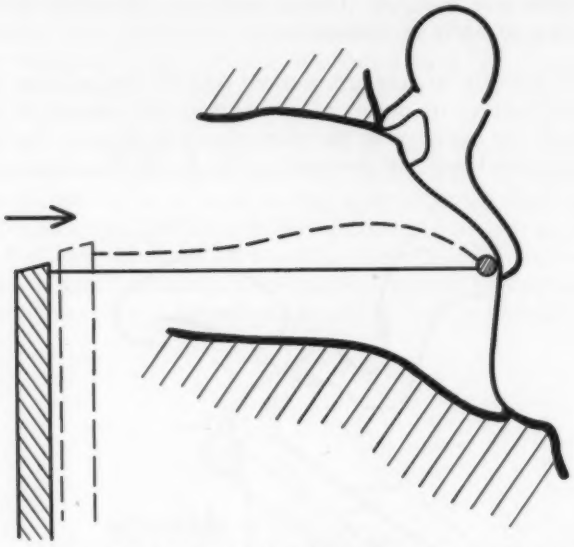


Fig. 6. Test hair for the production of normal pressure on the eardrum, taking advantage of the fact that the pressure produced by the test hair is not dependent upon the deformation of the hair.

thread is pressed against the eardrum, the pressure on the eardrum increases until the thread begins to bend. Further displacement of the handle does not affect the pressure against the eardrum. By pressing against the eardrum intermittently with this hair, one can observe the mobility of the ossicles for a given pressure. The maximum pressure produced by the test hair can be measured in grams on a balance.

It was possible to observe the movement of the stapes on many cadavers without difficulty, except when the ear canal was extremely narrow.

CONSTRUCTION OF AN ENDOTOSCOPE FOR SMALL HOLES.

The main problem in an endoscope is the illumination. If the tube of the endoscope contains a lens, it is generally impossible for the source of illumination to be in the same tube as that through which the observation is made, because light reflected on the surface of the lens is mixed with light from the surface being observed, and the contrast is decreased. We tried to decrease the reflections from the surface of the lens by coating it, but the results were not satisfactory. For this reason, most endoscopes use two tubes, one for observation, the other for illumination. This doubles the thickness of the endoscope.

Since what we wanted to avoid under any circumstances was unnecessary thickness, we attempted the difficult task of building a satisfactory endotoscope in which the same tube is used for observation and illumination, with no disturbing

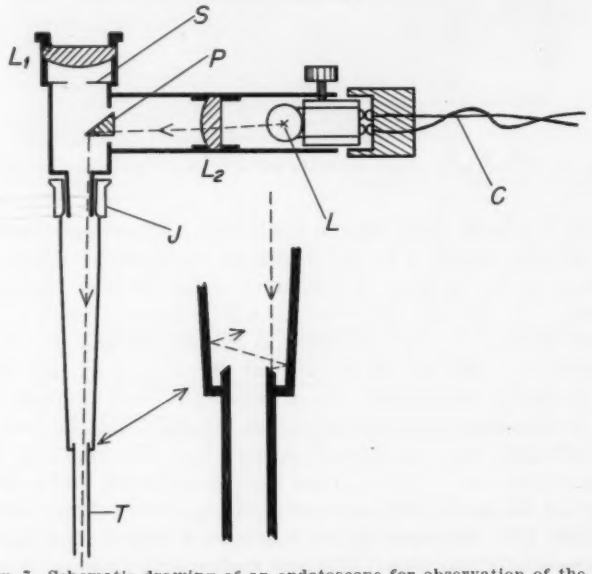


Fig. 7. Schematic drawing of an endotoscope for observation of the middle ear. The tube (T) can be reduced to an outside diameter of 1 to 2 mm., and these tubes can be easily interchanged.

reflections. A schematic drawing of the endotoscope developed is shown in Fig. 7, and a photograph of it is shown in Fig. 8. It was possible to reduce the outside diameter of the

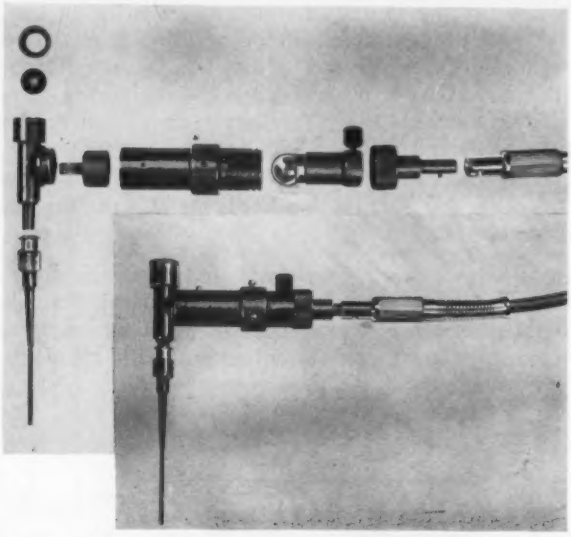


Fig. 8. Photographs of the separate parts of the endotoscope and of the instrument as finally assembled.

tube to 1.5 mm. This tube is made like a hypodermic needle, and can be attached to the T-shaped endotoscope simply by pushing it on, making sterilization quite simple. Having a number of slightly different, easily interchangeable tubes makes the endotoscope adaptable to many purposes. The focus of lens (L_1) was so adjusted that the object at the lower end of the tube appeared sharp. The light from a small bulb (L) was collected by lens (L_2) and directed into the tube by the left-hand edge of a small prism (P). The focus of lens (L_2) and the angle of the prism were so adjusted that a sharp image of the lamp filament was produced on the lower end of the tube (T), illuminating the whole field evenly. For a good observation of the object through such a small hole it seemed important to surround the field of view with a ring of com-

plete blackness. For this purpose, the upper end of tube (T) was beveled, as is shown by the enlarged details in Fig. 7. A light beam coming from the lamp is reflected on this beveled edge and absorbed on the side wall of the upper tube, which was covered with fine grooves. A special preparation, Ebonol C,[4] was used to obtain a completely black surface inside the tube, though the coat was less than 1/100 mm. thick. A special stop (S) was provided to eliminate scattered light in the upper parts of the tube.

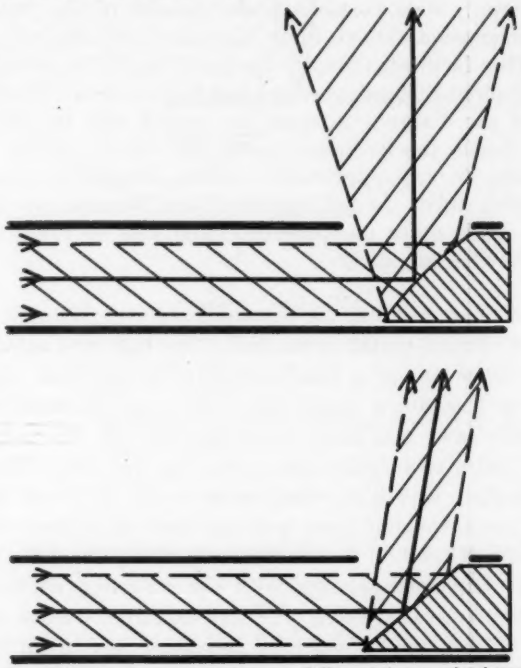


Fig. 9. In order to see around corners, different types of mirrors can be attached to the end of the tube of the endotoscope. The convex mirrors proved especially suitable.

Although at the beginning it seemed impossible to see much by looking through a tube with a diameter of 1 to 2 mm., the experiments demonstrated that after several hours' training it is possible to make out considerable detail.

In order to see around corners, small metal blocks with reflecting surfaces were attached to the end of the tube (see Fig. 9). Highly polished chrome plating was used for the reflecting surface. There are no disturbing light reflections from the illumination if the reflecting surfaces are kept reasonably clean. For a larger field of view a convex mirror can be attached to the end of the tube. This convex mirror proves very practical, because with a knowledge of the approximate sizes of the objects that we want to observe (*e.g.*, incus, stapes, etc.), it is possible, from the size of the images, to draw conclusions about their distance from the end of the tube. This facilitates greatly the handling of the endotoscope, since all other distance cues are lost in monocular observation. Because the distance between the object and the mirror is always small, the irregularities in the mirror do not distort the image to any appreciable extent; therefore, the interchangeable tubes do not require high-precision work; they can be made quite inexpensively, and can be thrown away when they become dirty.

The convex mirrors, for instance, were cut from a highly polished chrome-plated brass ball. The ball was attached to a lathe by means of a handle soldered to the ball. As illustrated in Fig. 10, a small tube with a saw-toothed cutting edge (hole saw) was used to cut sections from the ball. Each section had a clear reflecting surface on one side. The angle of the surface was determined by the angle of the cut into the ball. After several of these sections were cut around the ball, the center of the ball was drilled out (along the dotted line), and the cylindrical sections with the reflecting surfaces fell out. The diameter of these cylinders exactly fitted the opening in tube (T), so that it was then necessary only to cut them to the correct length.

The endotoscope was constructed in the machine shop of the Psycho-Acoustic Laboratory by Mr. Ralph Gerbrands. It has proved to be very successful for animal research, and we hope to try it out on patients.

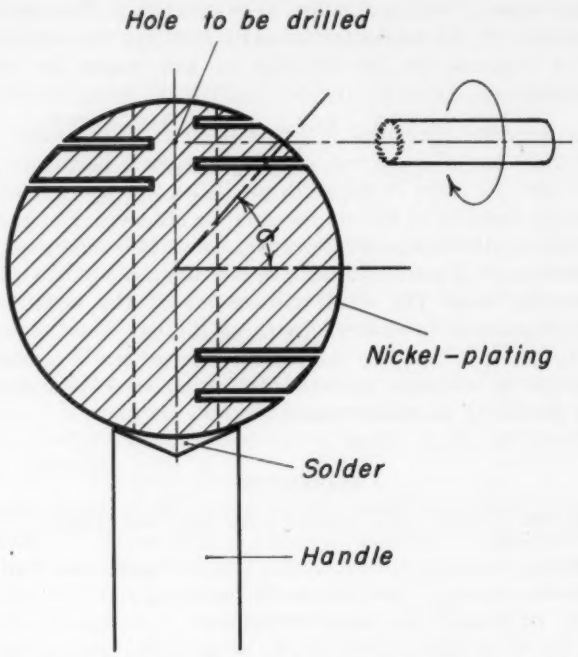


Fig. 10. Technique for cutting convex mirrors from a chromium plated ball.

SUMMARY.

This paper describes a method for the measurement of the transmission loss in anatomical preparations. If a patient's hearing loss is known, and it is possible, at a postmortem examination, to measure the conductive loss, then the difference between the two values is a measure of the nerve deafness. In this way we can separate the conduction loss from the nerve loss and express each in decibels. This makes it possible to determine the importance of different histological findings in the etiology of transmission deafness and nerve deafness.

Four cases of stapes fixation were measured. The decrease in mobility of the stapes for tones of 1000 cps was correlated with a decrease in the mobility of the stapes for static deformations.

For accurate diagnoses it seems possible to introduce into the middle ear a small endotoscope through a perforation of 1 to 2 mm. diameter in the eardrum. With this special endotoscope the mobility of the stapes could be observed, as has been demonstrated on anatomical preparations. It is supposed that this method will prove valuable in the diagnosis of the causes of hearing loss. The small dimensions of the endotoscope make it possible to observe parts of the ear canal that are usually inaccessible. For the examination of the ear canal of experimental animals (guinea pigs, rats, etc.) this endotoscope proved to be indispensable.

REFERENCES.

1. BEKESY, GEORG V.: *Akus. Ztschr.*, 7:173, 1942; *Jour. Acous. Soc. Am.*, 21:233-245, 1949.

2. BEKESY, GEORG V.: *Jour. Acous. Soc. Am.*, 20:749-760, 1948, Fig. 10.

3. BEKESY, GEORG V.: *Akus. Ztschr.*, 1:13, 1936, Fig. 7.

4. *Rev. of Scientific Instruments*, 19:826, 1948.

PROCAINE PENICILLIN SOLUTIONS IN THE TREATMENT OF NASAL POLYPOSIS.

SIMON L. RUSKIN, M.D.,
New York, N. Y.

Nasal polyposis has long been one of the most troublesome of the rhinologists' problems. In years past, the complete exenteration of the ethmoid labyrinth was the solution suggested by Halle, and Hajek proposed almost as radical an approach. The recognition of the part played by allergic reactions modified to a great extent the haste for radical surgery. Today it is realized that allergic sensitivity combined with chronic infection is the underlying factor in the causation of nasal polyposis.

Oskar Hisch should be given the credit for first pointing out that the antra were a frequent source for nasal polypi. The histopathology of nasal polypi show primarily two kinds: one, the soft polyp representing the thin sinus mucosa enormously distended by the accumulation of transudate. It is almost a single celled layer of epithelium holding back a volume of transudate, which it cannot absorb. The gradually increasing collection of transudate makes for perpetual growth of the polyp. The rate of absorption cannot keep pace with transudation. There are almost no glands in the sinus mucosa and only very slight secretion. The second type of polyp is the hard polyp formed from tissues of the lateral nasal wall, rich in glands and frequently cystic. This is not the type under consideration in this paper.

Removal of the soft polyp by snare has usually been followed by recurrence, while removal of the hard polyp along with the turbinate tissue from which it springs has less frequently been associated with recurrence.

Editor's Note: This ms. received in Laryngoscope Office and accepted for publication, Dec. 15, 1949.

To understand the mechanism and treatment of sinus polyposis, it is well to study not only the histologic appearance but also the reaction of the sinus membrane in the experimental animal. Fabricant has emphasized this in a short, excellent article on animal experimentation and nasal medication. He reported on the "studies which have been made of the absorptive ability of the mucous membrane of the dog's frontal sinuses by the introduction of drugs and other substances. Histamine, nicotine, ephedrine and epinephrine, drugs which institute rapid and pronounced alterations in blood pressure when injected intravenously, were found to be absorbed very slowly from the sinus mucous membrane. The absorption in fact was so slow that no definite changes in blood pressure were detected. A further experiment proved that the absorption from an inflamed mucous membrane is considerably more rapid than from a normal mucous membrane."

Fabricant also points out that "animal studies have demonstrated that various solutions of sodium and calcium penicillin (containing from 1,000 to 5,000 units per cubic centimeter) when applied topically to the respiratory nasal mucous membranes of rabbits every day for 30 to 90 days, have an apparently innocuous effect on nasal tissues. From these animal investigations and from numerous clinical reports on record it appears evident that penicillin solutions administered topically have no deleterious effect on respiratory nasal mucous membranes."

This experimental data is important in our approach to the treatment of nasal polyposis. It is obvious that the location to which treatment of polyposis must be directed is the sinus mucosa. If the transudation of fluid into the sinus subepithelial stroma can be controlled, the growth of the polyp would be stopped and resorption of the transudate slowly accomplished. To do this, a double action must be achieved; that is, the allergic reactivity must be reduced and the infection controlled. In previous years we combined vasoconstrictors with

antiseptics, which were used with only very limited benefit. The vasodilatation that followed the vasoconstriction counteracted the benefit of the whole therapy.

Procaine penicillin marked a turning point in nasal therapy. Here we have a preparation that has two active agents that uniquely enhance each other's action in a remarkable fashion. The procaine forms with the penicillin a salt procaine penicillin which is stable in solutions containing 1,000 to 5,000 units per cc. so that solutions can be used at room temperature without undergoing rapid hydrolysis and deterioration. These solutions may also be kept after preparation for prolonged periods. When sodium or potassium penicillin solutions are made hydrolysis sets in directly, since the sodium enters into a reversible reaction whereby sodium hydroxide is formed, which reacts with the penicillin to cause progressive deterioration. When, however, procaine penicillin is put into solution, the tendency to hydrolyze is negligible. It is this stable characteristic that makes it practically the ideal medication for instillation into the nasal sinuses.

The rate of absorption for the sinuses is so slow that when procaine penicillin solution of 3,000 to 5,000 units per cc. is instilled, it remains there for at least one to three days and, at times, a full week. This can be observed during the refilling when the slightly yellowish solution is displaced by the fresh solution. Frequently, crystals of procaine penicillin can be seen in the return flow a week after the original instillation.

Since procaine is an oil soluble base, its absorption by the mucosa is particularly slow, thus producing a depot action within the sinus. The presence of 3,000 to 5,000 units of penicillin in direct contact with the sinus mucosa for several days to a week produces a perfectly enormous dosage at the infected site. Usually one to two units per cc. of blood is considered adequate systemic dosage. In nasal polyposis, we are dealing with a localized infection that is practically not reached by systemic penicillin therapy at all. Higher dosages than 3,000 to 5,000 units per cc. within the sinus are not needed and would be wasteful. This prolonged effect for

procaine penicillin is not obtained with sodium penicillin since, at body temperature, sodium penicillin is hydrolyzed in three to four hours and the reservoir effect is not obtained.

Another factor of unique benefit in the procaine penicillin is the antihistamine action of procaine. This has not received all the attention it deserves. Frommel and his Swiss co-workers showed that procaine protected experimental animals against lethal doses of histamine aerosols and counteracted the effect of histamine on the terminal ileum. Clinically, it can be readily observed that following filling of the antra with procaine penicillin solutions there is decongestion of the mucosa of the lateral nasal wall with improved aeration of the nasal passages and improved drainage from the frontal, ethmoid and sphenoid sinuses. Filling of the sphenoid sinuses is an excellent collateral aid.

The antra are filled through the natural ostia. I use the Ruskin modification of the Yankauer cannula. This has simplified the technique considerably. For the preparation of the procaine penicillin solution, I add 20 cc. of procaine ascorbate solution to the vial containing 100,000 units of sodium penicillin. This forms the procaine penicillin and sodium ascorbate directly in the vial. The sodium ascorbate is useful in the solution since the ascorbate enhances penicillin action, as also shown by Jalili at Fuad University, and the ascorbate likewise has an antihistamine effect, as I have previously reported. An alternative method of preparation is the further dilution of the commercially available, ready to use, suspension solutions of procaine penicillin supplied by Squibb and Co., and Wyeth. One cubic centimeter of the solution-suspen-Co., and Wyeth. One cc. of the solution-suspension of procaine penicillin, containing 300,000 units, is diluted with two ounces (60 cc.) sterile saline. Ten cc. of this solution are instilled into each antrum and 5 cc. into each sphenoid sinus. Thus, one ounce is used for a complete treatment. This gives the patient 150,000 units in direct apposition to the sinus mucosa for a period actually of one to seven days. The use of the dilute solution in 10 cc. volume is preferable to high dosage such as the 300,000 units in 1 cc. because the 10 cc. produces

a continuous drip through the natural ostium, bathing the lateral nasal wall, nasopharynx and pharynx. This produces a generalized decongestion of the nasal mucosa. Under this treatment chronic sinus conditions of very long standing have shown striking improvement. It has, in my experience, eliminated sinus surgery to a remarkable degree.

The case here reported has been taken from a series of 60, to typify the results obtained.

Mr. I., age 60, had been suffering for over 20 years from recurrent sinus infections and polyposis. He had had three polypectomies and when advised to have a fourth, refused further surgery. At the time of the examination he was complaining of bilateral frontal headache, nasal discharge and nasal obstruction. His difficulties were worse at night when his nasal obstruction disturbed his sleep. He frequently was aroused several times during the night by the nasal obstruction. He had been using various nasal vasoconstrictors at night for years.

Nasal examination revealed multiple polypi in both middle meati, obstructing also both nasal fossae.

Following anesthetization of both sphenopalatine ganglia, each antrum was filled with 10 cc. of procaine penicillin solution containing 5,000 units per cc. prepared as above. This was repeated daily for three days, then every other day for six days and, after that, once weekly for two instillations. The patient also received simultaneous injections of calcium ascorbate (Calscorbate) intramuscularly. After the second day the patient reported that he was able to sleep through the night. The following refilling showed procaine penicillin crystals in the return flow. He felt very much more comfortable and, after one week, the polypi had shrunk to less than half their original size. After the third week the nose was clear and free from polypi. The patient was discharged and has remained free from nasal complaint or polyp recurrence for six months.

SUMMARY.

1. Nasal polyposis is amenable to conservative treatment by the use of solutions of procaine penicillin, 3,000 to 5,000 units per cc., when instilled into the nasal sinuses.

2. Procaine penicillin solutions provide a prolonged acting penicillin effect combined with the antihistaminic effect of procaine in decongesting the nasal mucosa. It is a great advance in nasal therapy.

32 East 67th Street.

BIBLIOGRAPHY.

FABRICANT, N. D.: Animal Experimentation and Nasal Medication. *Eye, Ear, Nose and Throat Mon.*, XXVII:283-284, June, 1948.

FROMMEL, E.; FAVRE, M., and VALLETTE, F.: *Arch. Intern. Pharmacodynami*, 73:355-366, 1947.

HAJEK, M.: Nebenhöken der Nase, Franz Deuticker, 1926.

HALLE, M.: Personal communication.

HISCH, O.: Personal communication.

JALILI, M. A.: Synergistic Effect of Vitamin C and B_2 on Penicillin. *Nature*, June 1, 1946.

RUSKIN, S. L.: Influence of Vitamin C on the Antihistamine Action of Various Drugs. *Arch. Otolaryngol.*, 36:853-873, 1942.

RUSKIN, S. L.: Studies on the Parallel Action of Vitamin C and Calcium. *Am. Jour. Dig. Dis.*, 10:170, 1943.

RUSKIN, S. L.: High Dosage Vitamin C in Allergy. *Am. Jour. Dig. Dis.*, 12:9, Sept., 1945.

DISLOCATION OF THE LARYNX.*†

LENNART GISSELSSON, M.D.,
Lund, Sweden.

Judging by the literature, dislocations of the larynx are very rare indeed. The joints between the cartilages of the larynx are rigid and well protected so that only a heavy blow or rather extreme compression will cause a dislocation of these joints. Laryngeal dislocations are as a rule caused by a direct blow against the larynx, when the resultant dislocation will most frequently be accompanied by a fracture of one of the cartilages. The joint most liable to dislocate is naturally the most flexible one, the cricoarytenoid. Only one case of dislocation of the cricothyroid articulation could be traced in the literature. Jackson and Jackson describe a man who, in an attempt to hang himself, dislocated both arytenoid cartilages and the cricothyroid articulation. The report of a further case, therefore, seems warranted.

CASE REPORT.

In an attempt to suppress a yawn, the patient, a 43-year-old man, had experienced a click in the larynx, and since then swallowing caused an intense pain in the left half of the throat. Examination showed that although the laryngeal prominence was still in the median plane, the posterior part of the thyroid cartilage protruded to the left. Laryngoscopy revealed the aryepiglottic fold to be somewhat extended on the right side but shortened on the left side. The voice and the movement of the vocal cords were apparently normal. The patient was X-rayed but no ossification of the laryngeal cartilages was observed, so that it was difficult to satisfactoriy explain his trouble. The only observation made was that the airway in the larynx was displaced to the left (see Fig. 1); however, on more careful palpation the inferior cornu of the thyroid cartilage could be felt on the left side, and it was found that this was

*Read at the meeting of the Swedish Otolaryngological Association, Stockholm, Sweden, November, 1947.

†From Department for Diseases of Nose, Throat and Ear of the University of Lund (Department Head: Prof. Gösta Dohlman).

Editor's Note: This ms. received in Laryngoscope Office and accepted for publication, Oct. 6, 1949.

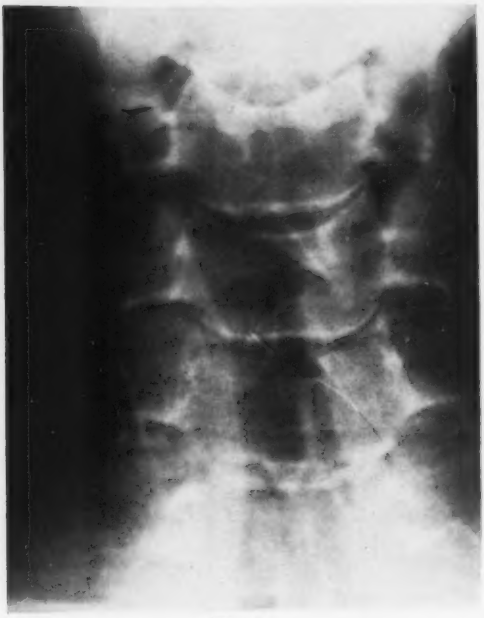


Fig. 1.

where the patient felt the pain. On the right side the inferior cornu could not be palpated; furthermore, the caudal margin of the thyroid cartilage with its inferior tubercle could be palpated on the left side but not on the right. The case was, therefore, diagnosed as a cricothyroidal dislocation. Local anesthesia was induced and pressure applied to the left side of the thyroid cartilage without any result, but when the right side of the thyroid cartilage was then lifted cranially and gentle pressure applied to the left side, a click was heard. The thyroid cartilage had snapped into normal position, and the patient was immediately able to swallow without discomfort. He was X-rayed again after this reposition, and the X-ray plate showed that the airway now passed straight through the larynx (see Fig. 2).

It must, therefore, have been a question of dislocation of the cricothyroid articulation and of the nature diagrammatically illustrated in the right sketch of Fig. 3. Why is this dislocation so rare? It is probably because in most individuals the joint between the thyroid and cricoid cartilages resembles more a symphysis than a joint in the general con-

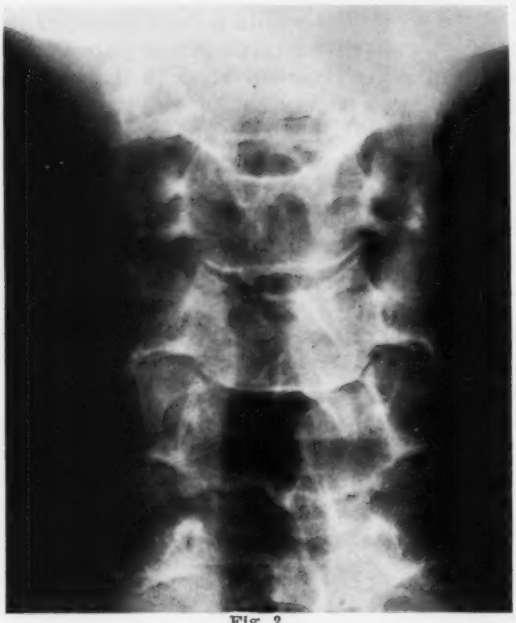


Fig. 2.

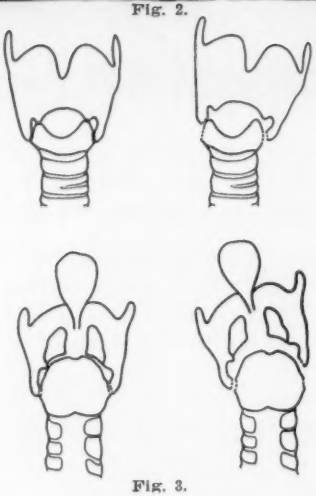


Fig. 3.

ception of the word. Cases with a fully developed joint have been described, even with a cartilaginous plate in the form of a disk between articulating surfaces. In the present case of laryngeal dislocation it must be a question of a proper joint, and the usually very tight ligaments in the capsule must be very elastic. Another reason why laryngeal dislocations are so rare is perhaps the unawareness of their occurrence. It is possible that some of the distinct pains in the throat which cannot be satisfactorily explained and are often diagnosed as neurosthenia, are some form of distortion or dysfunction in the cricothyroid joint.

REFERENCES.

JACKSON, C., and JACKSON, C. L.: *Arch. Otolaryngol.*, 38:413, 1943.

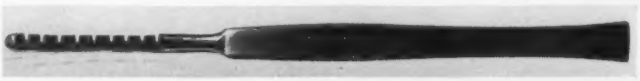
SCHUHMACHER, S.: *Wien. Klin. Wchnschr.*, 37:993, 1924.

A NEW BLUNT END STRAIGHT SAW-KNIFE FOR LOWERING A CARTILAGINOUS NASAL HUMP.*

M. WILLIAM MOOTNICK, M.D.,
New York, N. Y.

During my years of practice in the field of rhinoplasty, I occasionally encountered some technical difficulty in the correction involving a cartilaginous nasal hump and where the bony nasal bridge does not require any surgery, I found it very difficult or impossible to take a positive grip with an ordinary blunt end straight knife on the perichondrium covering the upper lateral cartilages, including the dorsal portion of the nasal septum.

To overcome this difficulty I decided to put teeth into the same instrument, enabling the latter to take a firm, positive



bite into the perichondrium covered cartilaginous hump with ease. The operative procedure may be completed with the saw knife or followed with the blunt end straight knife.

This instrument could also be used to advantage in lowering the cartilaginous portion of a normal profile after shortening the nasal tip in a long nose to make room for the excess nasal skin which thickens through contraction after operation.

11 West 42nd Street.

Editor"s Note: This ms. received in Laryngoscope Office and accepted for publication, Nov. 4, 1949.

KENFIELD MEMORIAL SCHOLARSHIP.

In 1937, a sum of money was subscribed in memory of Miss Coralie N. Kenfield, of San Francisco, Calif., a teacher well known throughout the United States for her high ideals and advanced methods in teaching lip reading. This money, placed in the Kenfield Memorial Fund, is administered by the American Hearing Society and provides for an annual scholarship. The amount of the Kenfield Memorial Scholarship for 1950 is $100.00.

Applications for the scholarship will be considered from any resident of the United States who desires to teach lip reading (speech reading), with or without other types of hearing, and speech therapy to the hard of hearing, and who can meet the following requirements:

Personal: Well adjusted individual with a pleasing personality, legible lips, a good speech pattern and no unpleasant mannerisms.

Education: College graduate with a major in education, psychology, and/or speech, plus professional training in lip reading; 30 clock hours of private instruction under an approved teacher of lip reading or 60 clock hours of instruction in public school classes under an approved teacher of lip reading.

The winner of the scholarship may take the teacher training course from any normal training teacher or school or university in the United States offering a course acceptable to the Teachers' Committee of the American Hearing Society. The scholarship must be used within one year from the date the award is made.

Applicants must be prospective teachers of lip reading to the hard of hearing. Those already teaching lip reading cannot be considered.

Applications must be filed between March 1 and May 1, 1950, with: Miss Rose V. Feilbach, Chairman, Teachers' Committee, 1157 North Columbus Street, Arlington, Va.

BOOK REVIEWS.

Public School Audiometry: Principles and Methods. By Loraine Anson Dahl, formerly Field Supervisor, Wisconsin State-Wide Hearing Survey; Supervisor, Hearng Test Service, Speech Clinic, Purdue University; Research Associate, Department of Otolaryngology, University of Iowa. With Foreword by Wendell Johnson, Ph.D., Director of Speech, University of Illinois. Two hundred ninety pages with Index and Bibliography. Danville, Ill.: The Interstate Printers and Publishers, 1949.

This book is made up of three principal parts: *1.* Factors to Be Considered in a Hearing Conservation Program, *2.* Creating Active Interest in the Conservation of Hearing, and *3.* Techniques and Principles of Audiometry. It also includes a Manual of Instruction of Audiometer Procedures in Public Audiometry, plus three sets of references.

The book should be helpful to those engaged in hearing conservation programs and to those who are on the periphery of such problems, such as health rehabilitation and guidance workers. The author is to be commended for emphasizing the follow-up in group testing which is too often neglected in public conservation programs. The suggestions for creating interest in a program of hearing conservation should be helpful to those who are inaugurating such a program. The forms at the end of the book should be very useful because they anticipate a great deal of detail involved in the program; however, the book leaves much to be desired, not so much because of what it says, but because of many errors of omission.

A perusal of the three bibliographies suggests that the author has failed to take adequate notice of recent developments in the field. This is surprising, since the book is dated June, 1949. Except for one or two items, the bibliography goes back to dates previous to 1944. Even if the author did not intend to cover some of the recent developments in detail, it would have been helpful to her readers to be guided to recent source material. A few illustrations of omission will serve to emphasize this point. In discussing classifications of audiograms, no mention is made of Carhart's useful method described in 1945. There is no reference to the Massachusetts Hearing Tests. Recent books which antedate the publication of this book, such as Brentano's book and the volume edited by Hallowell Davis, "Hearing and Deafness" are not mentioned. Under "periodicals" the author fails to include the *American Annals of the Deaf, Hearing News* and the *Journal of Exceptional Children.* In a survey of the "etiology" and "causes" of deafness, which ranges from congenital deafness in children to presbycusis in adults, it is surprising that no mention is made of otosclerosis or the fenestration operation. It would have been extremely valuable for the reader to have his attention called to recent developments in hearing aids and articulation tests, particularly as part of the follow-up program.

In the section on techniques and principles of audiometry nothing is said about the diagnostic value of bone conduction tests as part of the follow-up. In discussing the technique of testing in cases of unilateral impairment the author fails to point out the technique of masking.

There are also errors of proof-reading. For example, on page 287, which is the first page of the index, we have the reference "Davis, H." and on page 283 the same author is listed under the H's as "Hallowell, D." It is also amazing that the book has been put out without a table of contents. This reviewer could continue this list of omissions and inadequate treatment, both in the text and in the bibliography, but the examples given above indicate that the book is ready for some revision.

S. R. S.

Your Nasal Sinuses and Their Disorders. By Albert P. Seltzer, M.D., M.Sc., Sc.D.(Med.), F.A.C.S., F.I.C.S. Assistant Professor in Otolaryngology, Graduate School of Medicine, University of Pennsylvania; Assistant Otolaryngologist, Mt. Sinai Hospital, Philadelphia; Associate Chief in Ear, Nose and Throat, St. Luke's Medical Center; Chief of Staff in Plastic and Maxillo-Facial Surgery at Douglass-Mercy Hospital, Philadelphia; Chief of Staff of Plastic and Reconstructive Surgery, Community Hospital, Philadelphia. One hundred fifty-five pages with Index. New York, N. Y.: Froben Press, 1949. Price $2.50.

This book is presumably written for the laity. It carries one piece of advice, viz., "If you think you have sinusitis consult a nose and throat specialist," and two admonitions: *1.* "Don't diagnose your own case." *2.* "Don't treat yourself."

The author has used 152 pages and 24 illustrations to make these three points. One wonders what is accomplished by any discussion on the evolution and prenatal develoipment of the nose and sinuses in such a book—for the layman.

One questions the wisdom of a discussion in a textbook of this kind, of emotional factors in sinus disease, or of the symptomatology of sinusitis, as is done in the chapter entitled, "What Is Your Complaint?" Surely this is urging the layman to make his own diagnosis, and the patient, with the little knowledge gleaned from this book becomes a nuisance to the otolaryngologist whom he finally consults.

The 24 illustrations are mostiy without point, are undignified and have nothing to recommend them.

All in all, it seems this book will do more harm than good.

T. E. W.

HEARING AIDS ACCEPTED BY THE COUNCIL ON PHYSICAL MEDICINE OF THE AMERICAN MEDICAL ASSOCIATION.

As of January 1, 1950.

Aurex Model F and Model H.
Manufacturer: Aurex Corp., 1117 N. Franklin St., Chicago, Ill.

Beltone Mono-Pac; Beltone Harmony Mono-Pac; Beltone Symphonette.
Manufacturer: Beltone Hearing Aid Co., 1450 W. 19th St., Chicago, Ill.

Dysonic Model 1.
Manufacturer: Dynamic Hearing Aids, 43 Exchange Pl., New York 5, N. Y.

Electroear Model C.
Manufacturer: American Earphone Co., Inc., 10 East 43rd St., New York 17, N. Y.

Gem Hearing Aid Model V-35.
Manufacturer: Gem Ear Phone Co., Inc., 50 W. 29th St., New York 1, N. Y.

Maico Type K; Maico Atomeer.
Manufacturer: Maico Co., Inc., North Third St., Minneapolis, Minn.

Mears Aurophone Model 200; 1947—Mears Aurophone Model 98.
Manufacturer: Mears Radio Hearing Device Corp., 1 W. 34th St., New York, N. Y.

Micronic Model 101 (Magnetic Receiver); Micronic Model 303. (See Silver Micronic.)
Manufacturer: Micronic Co., 727 Atlantic Ave., Boston 11, Mass.

Microtone T-3 Audiomatic; Microtone T-4 Audiomatic; Microtone T-5 Audiomatic.

Manufacturer: Microtone Co., 4602 Nicollet Ave., Minneapolis 9, Minn.

National Cub Model; National Standard Model; National Star Model.

Manufacturer: National Hearing Aid Laboratories, 815 S. Hill St., Los Angeles 14, Calif.

Otarion Model E-1; Otarion Model E-1S; Otarion Model E-2; Otarion Model E-4.

Manufacturer: Otarion Hearing Aids, 159 N. Dearborn St., Chicago, Ill.

Paravox Models VH and VL; Paravox Model XT; Paravox Model XTS; Paravox Model Y (YM, YC and YC-7).

Manufacturer: Paraphone Hearing Aid, Inc., 2056 E. 4th St., Cleveland, Ohio.

Radioear 45-CM; Radioear Model 45-M-magnetic air conduction receiver; Radioear Model 45-M-magnetic bone conduction receiver; Radioear Permo-Magnetic Uniphone; Radioear Permo-Magnetic Multipower.

Manufacturer: E. A. Myers & Sons, 306 Beverly Rd., Mt. Lebanon, Pittsburgh, Pa.

Silver Micronic Hearing Aid Model 101; Silver Micronic Hearing Aid Models 202M and 202C. (See Micronic.)

Manufacturer: Micronic Corp., 101 Tremont St., Boston 8, Mass.

Silvertone Model 103BM.

Distributor: Sears-Roebuck & Co., Chicago, Ill.

Sonotone Model 600; Sonotone Model 700; Sonotone Model 900; Sonotone Models 910 and 920.

Manufacturer: Sonotone Corp., Elmsford, N. Y.

Superfonic Hearing Aid.

Manufacturer: American Sound Products, Inc., 2454 S. Michigan Ave., Chicago, Ill.

Televox Model E.

Manufacturer: Televox Mfg. Co., 117 S. Broad St., Philadelphia 7, Pa.

Telex Model 22; Telex Model 97; Telex Model 99; Telex Model 1700.

Manufacturer: Telex, Inc., Minneapolis 1, Minn.

Tonemaster Model Royal.

Manufacturer: Tonemasters, Inc., 1627 Pacific Ave., Dallas 1, Tex.

Trimm Vacuum Tube No. 300.

Manufacturer: Trimm, Inc., 400 W. Lake St., Libertyville, Ill.

Unex Model "A"; Unex Midget Model 95; Unex Midget Model 110.

Manufacturer: Nichols & Clark, Hathorne, Mass.

Vacolite Model J.

Manufacturer: Vacolite Co., 3003 N. Henderson St., Dallas 6, Tex.

Western Electric Model 63; Western Electric Model 64; Western Electric Models 65 and 66.

Manufacturer: Western Electric Co., Inc., 120 Broadway, New York 5, N. Y.

Zenith Radionic Model A-2-A; Zenith Radionic Model A-3-A; Zenith Radionic Model B-3-A; Zenith Model 75; Zenith Miniature 75.

Manufacturer: Zenith Radio Corp., 6001 Dickens Ave., Chicago, Ill.

All of the accepted hearing devices employ vacuum tubes.

Accepted Hearing Aids more than five years old have been omitted from this list for brevity.

TABLE HEARING AIDS.

Aurex (Semi-Portable)—*Jour. A. M. A.*, 109:585 (Aug. 21), 1937.

Manufacturer: Aurex Corp., 1117 N. Franklin St., Chicago (10), Ill.

Precision Table Hearing Aid—*Jour. A. M. A.*, 139:785-786 (Mar. 19), 1949.

Manufacturer: Precision Electronics Co., 850 West Oakdale Ave., Chicago 14, Ill.

Ravox—*Jour. A. M. A.*, 113:18 (Oct. 28), 1939.

Manufacturer: Zenith Radio Corp., 6001 W. Dickens Ave., Chicago, Ill.

Sonotone Professional Table Set Model 50—*Jour. A. M. A.*, 141:658 (Nov. 15), 1949.

Manufacturer: Sonotone Corp., Elmsford, N. Y.

All of the Accepted hearing devices employ vacuum tubes.

DIRECTORY OF OTOLARYNGOLOGIC SOCIETIES.

AMERICAN OTOLOGICAL SOCIETY.

President: Dr. Philip E. Meltzer, 20 Charlesgate, West Boston 15, Mass.
Secretary: Dr. Gordon D. Hoople, Medical Arts Bldg., Syracuse 3, N. Y.
Meeting: Mark Hopkins Hotel, San Francisco, Calif., May, 1950.

AMERICAN LARYNGOLOGICAL ASSOCIATION.

President: Dr. Ralph A. Fenton, 906 Medical Arts Bldg., Portland, Ore.
Secretary: Louis H. Clerf, 1530 Locust St., Philadelphia 2, Pa.
Meeting: Mark Hopkins Hotel, San Francisco, Calif., May, 1950.

AMERICAN LARYNGOLOGICAL, RHINOLOGICAL AND OTOLOGICAL SOCIETY, INC.

President: Dr. Robert C. Martin, 384 Post St., San Francisco 8, Calif.
Secretary: Dr. C. Stewart Nash, 708 Medical Arts Building, Rochester, N. Y.
Meeting: Mark Hopkins Hotel, San Francisco, Calif., May, 1950.

AMERICAN LARYNGOLOGICAL, RHINOLOGICAL AND OTOLOGICAL SOCIETY, INC.

Eastern Section, Hotel Statler, New York, N. Y., Jan. 5, 1950.
Council Meeting, Hotel Statler, New York City, Jan. 6, 1950.
Combined Meeting, Southern and Middle Sections, Peabody Hotel, Memphis, Tenn., Jan. 16-17, 1950.
Western Section, Medical Society Bulding, Los Angeles, Calif., Jan. 21-22, 1950.

AMERICAN MEDICAL ASSOCIATION, SECTION ON LARYNGOLOGY, OTOLOGY AND RHINOLOGY.

Chairman: Dr. William R. Johnston, 1515 State St., Santa Barbara, Calif.
Secretary: Dr. James M. Robb, 641 David Whitney Bldg., Detroit, Mich.

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY.

President: Dr. J. Mackenzie Brown, 1136 W. 6th St., Los Angeles, Calif.
President-Elect:
Executive Secretary: Dr. William L. Benedict, Mayo Clinic, Rochester, Minn.

AMERICAN SOCIETY OF OPHTHALMOLOGIC AND OTOLARYNGOLOGIC ALLERGY.

President: Dr. George E. Shambaugh, Jr., 55 E. Washington St., Chicago, Ill.

President-Elect: Dr. Wm. H. Evans, 24 Wick Ave., Youngstown, Ohio.

Secretary-Treasurer: Dr. Joseph Hampsey, 806 May Bldg., Pittsburgh 22, Pa.

PAN AMERICAN ASSOCIATION OF OTO-RHINO-LARYNGOLOGY AND BRONCHO-ESOPHAGOLOGY.

President: Prof. Justo Alonso.

Secretary: Dr. Chevalier L. Jackson, 255 S. 17th St., Philadelphia, Pa.

Second Pan American Congress of Oto-Rhino-Laryngology and Broncho-Esophagology: Montevideo, January, 1950.

AMERICAN BRONCHO-ESOPHAGOLOGICAL ASSOCIATION.

President: Dr. LeRoy A. Schall, 243 Charles St., Boston, Mass.

Secretary: Dr. Edwin N. Broyles, 1100 N. Charles St., Baltimore 1, Md.

Meeting: Mark Hopkins Hotel, San Francisco, Calif., May, 1950.

LOS ANGELES SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY.

President: Dr. Warren A. Wilson.

Secretary-Treasurer: Dr. Victor Goodhill.

Chairman of Section on Ophthalmology: Dr. George Landegger.

Secretary of Section on Ophthalmology: Dr. Harold B. Alexander.

Chairman of Section on Otolaryngology: Dr. Alden H. Miller.

Secretary of Section on Otolaryngology: Dr. Leland R. House.

Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd., Los Angeles, Calif.

Time: 6 P.M., fourth Monday of each month from September to May, inclusive.

AMERICAN OTORHINOLOGIC SOCIETY FOR THE ADVANCEMENT OF PLASTIC AND RECONSTRUCTIVE SURGERY.

President: Dr. Alfred Schattner, 115 E. 61st Street, New York 21, N. Y.

Secretary: Dr. Norman N. Smith, 291 Whitney Avenue, New Haven 11, Conn.

WEST VIRGINIA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY.

President: Dr. Garnett P. Morison, Charles Town, W. V.

First Vice-President: Dr. Charles T. St. Clair, Jr., Bluefield, W. Va.

Second Vice-President: Dr. Arthur C. Chandler, Charleston, W. Va.

Secretary: Dr. Melvin W. McGehee, 425 Eleventh St., Huntington 1, W. Va.

Treasurer: Dr. Frederick C. Reel, Charleston, W. Va.

Directors: Dr. Eugene C. Hartman, Parkersburg, W. Va.; Dr. Ivan Fawcett, Wheeling, W. Va.

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY.

President: Dr. David R. Higbee, 3245 4th St., San Diego, Calif.
Secretary-Treasurer: Dr. C. Allen Dickey, 450 Sutter St., San Francisco, Calif.
Meeting: St. Francis Hotel, San Francisco, Calif., May 28-31, 1950.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Dr. Alston Callahan, 908 S. 20th St., Birmingham, Ala.
Chairman-Elect: Dr. Francis LeJeune, Ochsner Clinic, New Orleans, La.
Vice-Chairman: Dr. Edwin Broyles, 1100 N. Charles St., Baltimore, Md.
Secretary: Dr. Edley H. Jones, 1301 Washington St., Vicksburg, Miss.
Next Meeting: St. Louis, Mo., Nov. 13-16, 1950.

THE PHILADELPHIA LARYNGOLOGICAL SOCIETY.

President: Dr. M. Valentine Miller, 114 W. Phil-Ellen St., Philadelphia, Pa.
Vice-President: Dr. Thomas F. Furlong, Jr., 36 Parking Plaza, Ardmore, Pa.
Treasurer: Dr. Harry P. Schenck, 1912 Spruce St., Philadelphia, Pa.
Secretary: Dr. William J. Hitschler, 5 E. Chestnut Hill Ave., Philadelphia 18, Pa.

SOCIEDAD NACIONAL DE CIRUGIA OF CUBA.

Presidente: Dr. Reinaldo de Villiers.
Vicepresidente: Dr. César Cabrera Calderin.
Secretario: Dr. José Xirau.
Tesorero: Dr. Alfredo M. Petit.
Vocal: Dr. José Gross.
Vocal: Dr. Pedro Hernández Gonzalo.

ASSOCIACAO MEDICA DO INSTITUTO PENIDO BURNIER — CAMPINAS.

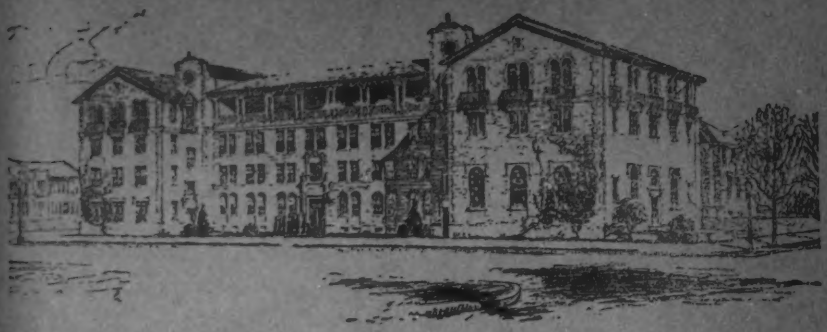
President: Dr. Joao Penido Burnier.
First Secretary: Dr. Gabriel Porto.
Second Secretary: Dr. Roberto Barbosa.
Librarian-Treasurer: Dr. Leoncio de Souza Queiroz.
Editors for the Archives of the Society: Dr. Guedes de Melo Filho, Dr. F. J. Monteiro Sales and Dr. Jose Martins Rocha.

SOCIEDAD DE OTORRINOLARINGOLOGIA Y BRONCOESOFAGOSCOPIA DE CORDOBA.

Presidente: Dr. Aldo Remorino.
Vice-Presidente: Dr. Luis E. Olsen.
Secretario: Dr. Eugenio Romero Díaz.
Tesorero: Dr. Juan Manuel Pradales.
Vocales: Dr. Osvaldo Suárez, Dr. Nondier Asís R., Dr. Jorge Bergallo Yofre.

BUENOS AIRES CLUB OTORINOLARINGOLOGICO.

Presidente: Dr. Juan Manuel Tato.
Vice-Presidente: Dr. Norberto Von Soubiron.
Secretario: Dr. Oreste E. Bergaglio.
Pro-Secretario: Dr. Carlos A. Gutierrez.
Tesorero: Dr. Vicente R. Carri.
Pro-Tesorero: Dr. Jorge Couzo.



Central Institute for the Deaf

NATIONAL RESIDENTIAL AND DAY SCHOOL FOR THE DEAF AND DEFECTIVES IN SPEECH

Approved by Advisory Council of Foremost Ear Specialists and Educators

New fire-proof buildings beautifully located opposite Forest Park. Modern Dormitories and Equipment. Best home environments. Pupils constantly in care of teachers or experienced supervisors.

ORAL SCHOOL FOR DEAF CHILDREN

C. I. D. offers all advantages of exclusively Speech Training and expert medical supervision for both Resident and Day Pupils.
Nursery School (2 years of age) through the Elementary Grades.

ACOUSTIC TRAINING FOR CHILDREN WITH RESIDUAL HEARING

Salvaging of Residual Hearing is a specialty of C. I. D. The Acoustic Method was created here. Group and individual hearing aids used for class instruction at all grade levels.

LIP-READING INSTRUCTION

Private and Class Instruction for Hard-of-Hearing Adults and Children.
Conversational Classes for advanced pupils. Speech conservation stressed.

CORRECTION OF SPEECH DEFECTS

Private and Class Instruction for children with normal hearing and delayed speech or defective speech.
Resident and Day Pupils (2 years of age through Elementary Grades).
Private Instruction for Adults.
Correction of Imperfect Phonation, Imperfect Articulation, Aphasia, Stuttering.

TEACHERS TRAINING COLLEGE

Two years of Training following a professional curriculum for applicants with adequate college qualifications. Graduates qualify for degrees of Bachelor of Science in Education or Master of Science in Education from Washington University. Graduates prepared to teach both the deaf and speech defective.

DR. MAX A. GOLDSTEIN, Founder - MISS JULIA M. CONNERY, Principal Emeritus

For further information address

DR. HELEN SCHICK LANE, Principal

818 S. KINGSHIGHWAY 10, ST. LOUIS, MO.

CONTENTS